December 8, 2006

BY ELECTRONIC DELIVERY

Attention: Deborah Perfetto
United States Pharmacopeia
Model Guidelines Submissions
Department of Information Development
12601 Twinbrook Parkway
Rockville, MD 20852-1790

Re: Comments on the Draft Medicare Model Guidelines Version 3.0

Dear Ms. Perfetto:

The Biotechnology Industry Organization (BIO) appreciates this opportunity to comment on the United States Pharmacopeia's (USP) Draft Medicare Model Guidelines Version 3.0 (Revised Guidelines). BIO is the largest trade organization to serve the biotechnology industry in the United States and worldwide, and represents more than 1,100 biotechnology companies, academic institutions, state biotechnology centers, and related organizations in the United States. Our members are involved in the research and development of healthcare, agriculture, industrial and environmental biotechnology products, with over 300 biotech drugs in clinical development addressing cancer, heart disease, Parkinson's, Alzheimer's and other intractable diseases. BIO generally supports the comments to the Revised Guidelines submitted by our various members, but also writes separately with regard to specific concerns we have as an industry organization.

BIO appreciates the time and effort that the USP and the Model Guidelines Expert Committee (MGEC) have devoted to developing the Revised Guidelines. We particularly are pleased that the USP is proposing the addition of 11 pharmacological classes and the expansion of the number of Formulary Key Drug Types (FKDTs) from 141 to 186. BIO continues to believe that increased granularity is critical to ensuring that Medicare

beneficiaries have access to the prescription therapies they need most. As a result, we recommend that USP, at a minimum, finalize the proposed additional classes and FKDTs except as noted in the comments that follow.

BIO has reviewed and considered the Revised Guidelines and has identified a few areas of continuing concern. Specifically, BIO recommends that (i) USP continue to implement a timely and responsive review process to ensure that beneficiaries have access to new therapies and new indications and to provide increased transparency as to the rationale supporting USP's revisions to the Model Guidelines; and (ii) USP continue to expand the classes and categories in the Revised Guidelines to ensure full access to Part D drugs and biologicals by beneficiaries. BIO requests that USP consider these recommendations as it finalizes the Revised Guidelines.

I. Process for Updating the Model Guidelines to Incorporate New Therapies and Indications

BIO recognizes and appreciates the changes USP has made to the process for monitoring and updating the Model Guidelines to incorporate newly approved therapies. For example, we applaud USP for providing brief synopses explaining the MCEG decisions in a chart released at the time USP released version 2.0, for providing more specificity regarding the quarterly review process, and for the more predictable timeframes for the development of version 3.0. Although BIO believes that these elements of the Model Guidelines procedure should continue, there remains room for improvement in the timeliness and transparency of the process.

Ensuring that the categories, classes, FKDTs, and drug listings for the Model Guidelines remain current is critical. The inclusion of Sitagliptin, approved by the Food and Drug Administration (FDA) in October, as an example of an agent within the "Dipeptidyl Peptidase-4 (DPP-4) Inhibitors" FKDT reflects that USP's review process is staying current with developments relating to new Part D drugs and biologicals. This responsiveness will be particularly important with respect to new therapies and indications that are approved by the FDA after the period for commenting on the Revised Guidelines has closed, and that potentially may warrant establishment of a new class or category. BIO asks USP, prior to finalizing version 3.0, to review the latest approvals from the FDA and assess the need for changes to the Revised Guidelines.

Moreover, USP needs to provide a better explanation of how it will respond to newly approved products or indications after the release of version 3.0. BIO believes that USP should use its quarterly review process to consider newly approved products and indications and issue public statements as to how those products or indications would fit within the Model Guidelines. That would assist the Centers for Medicare and Medicaid Services (CMS) in its efforts to ensure that Part D plans are responsive to newly approved therapies or indications, facilitating access by Medicare beneficiaries to new innovations and state-of-the-art care.

BIO also recognizes and appreciates the increased transparency USP has provided on the methodology for reviewing the Model Guidelines, but believes that USP can do more in this regard. As noted above, we found the explanatory synopses released with version 2.0 to be very useful. BIO asks that USP extend the utility of this concept to the release of a draft of the Model Guidelines, however. That can help the public understand the MCEG's bases for its decisions, yielding more informed comments on the draft revisions. BIO believes that final revisions will be improved as a result.

In addition, BIO renews its request that USP publish materials explaining what information it has examined and considered in reviewing new drugs and biologicals and its rationale for determining a new treatment's therapeutic category, pharmacological class or classification, or for not including a particular therapy at all. We also urge USP to provide a greater level of transparency to the quarterly review process. USP should identify what issues are on the agenda for each quarterly review, identify the comments submitted for each quarterly review, and make any determinations that emerge from its new quarterly review process available to the public through its web site.

II. The Model Guidelines Should Serve Their Intended Purpose of Ensuring That Beneficiaries Have Access to Needed Therapies

BIO renews its recommendation that the Model Guidelines should serve to promote beneficiary access to Part D covered therapies, particularly because the Model Guidelines will afford some protection from CMS' review of plan formularies. BIO continues to believe that the USP's focus in revising the Model Guidelines should be to ensure that the

categories and classes will prevent a plan from discouraging enrollment of certain types of beneficiaries with particular conditions or diseases.

BIO recognizes and applauds the changes USP has made in the Revised Guidelines to increase the granularity of the classes and categories, such as the establishment of a new FKDT for echinocandin antifungals. In our comments on the draft of version 2.0 of the Model Guidelines, we explained that the echinocandin class of anti-fungal products treat very serious invasive fungal infections that, if untreated or treated inappropriately, could result in extended hospitalization or death. Although USP did not make this change in version 2.0, we were pleased to see it proposed for version 3.0. BIO supports the creation of a new FKDT for echinocandin antifungals that is separate from the "Antifungals (Other)" FKDT and urges USP to finalize this change.

BIO also supports USP's inclusion of 13 new FKDTs in the "Enzyme Replacements/Modifiers" therapeutic category. As we emphasized in our comments on version 2.0 of the Model Guidelines, each disease in the Enzyme Replacements/Modifiers category is a rare disease caused by a unique deficiency or problem, and treatments are not interchangeable among patients with different diseases. If these treatments are not separately classified, Medicare beneficiaries with rare disorders may not have access to the therapy that addresses their unique clinical problems. Accordingly, BIO agrees with the addition of the new FKDTs in the Enzyme Replacements/Modifiers category and strongly encourages USP to finalize this change.

BIO also applauds the increase in the number of FKDTs for vaccines in the Immunological Agents category. This increased granularity will help to ensure beneficiary access to the wide range of vaccines that target diseases in the aged and disabled Medicare population, and BIO urges USP to finalize the addition of these new FKDTs.

BIO further supports USP's intent, based on explicit CMS guidance, to include all Part B antineoplastic drugs which could conceivably be administered in a long-term care setting and therefore be covered under the Medicare Part D benefit.[1] We assume that this was USP's rationale for

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[1] Williams RL and Perfetto D, "Changes in USP Model Guidelines for Medicare Plans in 2008," during Question and Answer session at BIO, 1225 Eye St, NW, Washington, DC, November 28, 2006.

adding the pharmacologic class Monoclonal Antibodies (MoAb) to Version 3.0. However, we would greatly appreciate further guidance behind the rationale underlying the specific placement of MoAb antibodies. These innovative therapies treat many types of diseases using many different mechanisms of action. With further guidance from USP, BIO can provide detailed comments on clinical appropriateness. In the meantime, BIO urges USP to add further granularity with additional FKDTs in the proposed MoAb and Immunodulators, Other classes to "ensure that a formulary is complete and will not substantially discourage enrollment of eligible beneficiaries."[2]

Because each MoAb targets a specific antigen, different MoAbs are required depending on which antigen a particular type of cancer cell expresses, to ensure that Medicare beneficiaries receive the most clinically appropriate therapy for their tumor type. It would be inappropriate to include an FKDT for anti-CD20 antibodies while excluding other targeted antineoplastic therapies used by the Medicare population, such as those that target CD52, EGFR, HER2 and VEGF, indicated for a variety of different cancers including breast, colorectal, lung and leukemia. For Version 3.0, we believe these MoAbs require their own FKDTs, specific to their targeted antigens.. Similarly, USP should create a separate FKDT for Natalizumab in the Immunodulators, Other class because of its unique mechanism of action directed against the α4 Integrin molecule.

Regarding pharmacologic class entitled, "Immune Suppressants," BIO is concerned that the draft Model Guidelines do not accurately reflect how immune suppressants are used by Medicare beneficiaries. Currently, the pharmacologic class titled "Immune Suppressants" has only two FKDTs: (1) "TNF Inhibitors" and (2) "Non-TNF Inhibitors." However, the therapies included in the FKDT "Non-TNF Inhibitors" are not therapeutically interchangeable, as these drugs are used to treat patients with various medical conditions and one drug can not necessarily be substituted with another. The FKDTs should be expanded to ensure that Medicare Part D formularies are complete, are consistent with CMS' "All or Substantially All" policy, and therefore do not discourage

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[2] United States Pharmacopeial Convention, Model Guidelines Version 2.0: Preamble, February 6, 2006, p. 2.

enrollment because products for certain conditions are not included in the formulary.

BIO remains concerned that additional categories or classes are necessary to account for distinct therapies with clinically relevant differences, such as selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs). We are aware that a number of parties submitted comments on version 2.0 of the Model Guidelines opposing the reclassification of the FKDTs for SSRIs and SNRIs into a single pharmacological class. The MGEC concluded based on an understanding of available comparative safety and efficacy information that these categories were clinically non-distinct. BIO respectfully disagrees with this determination and strongly encourages USP to consider the extensive clinical evidence that others have submitted on the differences between SSRIs and SNRIs in the treatment of depression and that may be submitted in response to the Revised Guidelines. Creating two separate pharmacological classes for these agents in the Antidepressant therapeutic category will better ensure that beneficiaries suffering from depression have access to the treatment most appropriate for them.

We note that USP has added a pharmacologic class for "Anti-HIV Agents, Combinations" and unfortunately view this class as insufficient to help protect the interests of HIV/AIDS patients. Rather, we urge USP to add a separate pharmacologic class to the anti-HIV agents named "Anti-HIV Agents, Single Tablet Regimen (STR)**"** to include multi-class antiretroviral medications such as efavirenz/emtricitabine/tenofovir disoproxil fumarate. This multi-class antiretroviral agent in one single tablet has been recognized by the FDA as a new class and may also serve as a complete regimen for the treatment of HIV disease, with the components recognized by HHS guidelines. Adding this separate class would help ensure that the Model Guideline satisfy the statutory protection that prevents plans from discouraging enrollment of HIV/AIDS patients since the availability of simplified therapies should help encourage more patients to seek treatment.

USP's practice of including certain combination drugs in the Model Guidelines but not others concerns BIO as the practice could be perceived as suggesting that the listed combination drugs are more deserving of coverage under Part D than non- listed combination drugs. BIO will begin to further explore this issue and looks forward to working with USP during 2007, such that the next year's update appropriately includes all combination therapies.

IV. Conclusion

BIO applauds the changes made to the Revised Guidelines and appreciates this opportunity to comment on issues of ongoing concern. We look forward to continuing to work with the USP and CMS to revise and refine the Model Guidelines to ensure that Medicare beneficiaries have access to critical Part D drugs and biologicals.

Respectfully submitted,

/s/

Jayson Slotnik,
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& Economic Policy
Biotechnology Industry Organization