January 6, 2006

BY ELECTRONIC DELIVERY

Attention: Deborah Perfetto
United States Pharmacopeia
12601 Twinbrook Parkway
Rockville, MD 20852-1790

Re: Comments on the Revised Model Guidelines

Dear Ms. Perfetto:

The Biotechnology Industry Organization ("BIO") appreciates the opportunity to comment on the United States Pharmacopeia's ("USP") Medicare Prescription Drug Benefit Model Guidelines Version 2.0 ("Revised Guidelines") that were released this month. 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 condensed time frame that the USP and the Model Guidelines Expert Committee (MGEC) had to develop the Revised Guidelines and their supportive documents. We are pleased that the USP has developed the comprehensive drug listing to demonstrate how drugs would be categorized and that the USP has provided the Centers for Medicare and Medicaid Services ("CMS") with Formulary Key Drug Types ("FKDTs") as a "check" to assess whether a particular formulary includes at least one drug from each item in the listing. BIO firmly believes that increased access to prescription therapies will improve the overall health of Medicare beneficiaries and that this can be realized, in part, by the USP's further revisions to the Model Guidelines, particularly if more granularity is provided.

BIO carefully has reviewed and considered the Revised Guidelines, and there are a number of issues that concern us. We already raised several of these concerns in our comments to the initial Model Guidelines. BIO continues to believe strongly that the Model Guidelines should include formulary classes and categories that will ensure full access to Part D drugs and biologicals by beneficiaries. Accordingly, BIO recommends that (i) the formulary classes and categories be further expanded to include new categories or classes for the clinically important therapies that do not currently fall within any existing category or class; (ii) a mechanism be created for incorporating drugs and biologicals that are used to treat rare disorders that are not otherwise included in existing classes and categories; and (iii) the USP update the Model Guidelines more frequently, with public input, and with a transparent process.

Specifically, BIO urges the USP to release a comprehensive list of the types and sources of information reviewed and the decision rationale used during the update process. BIO asks for greater transparency and clarity regarding your decision process. We are concerned about the vagueness of your preamble language that is used to describe the criteria for revision. Finally, BIO asks for USP to begin a public dialogue to elicit comments on how to create a more predictable process for the next Model Guidelines update. BIO believes that our recommendations will ensure that

beneficiaries have immediate and continued access to new therapies and existing therapies with new indications.

I. 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 ensure access to Part D drugs and biologicals, particularly because the Model Guidelines will afford some protection from CMS' review of plan formularies. BIO strongly believes that the USP's continuing 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.

We recognize that USP has made some changes in the Revised Guidelines to provide some additional granularity. BIO is pleased that the USP created a specific class for "Phosphate Binders" under the therapeutic category of Genitourinary Agents. The need for phosphate binder categories or classes was identified by the End Stage Renal Disease (ESRD) Outpatient Medications Project recently completed for CMS by ESRD Network 8, Inc. and the University of Mississippi. This project was conducted for CMS to identify medications that should always be available for ESRD patients and to help CMS understand the implications of decisions and benefit design of Part D drug plans on the ESRD population.

However, BIO has an issue with the echinocandin class of anti-fungal products. These products generally treat very serious invasive fungal infections that, if untreated or not treated appropriately, could result in extended hospitalization and/or death of the patient. The other anti-fungal products currently included in the "antifungal (other)" classification are topical creams/ointments used to treat non-life threatening dermatological infections. Therefore we believe that the current class inappropriately groups very different therapies. We therefore propose to pull the echinocandin products out the "antifungal (other)" group and establish a new key drug type group for them (*e.g.*, "echinocandin antifungals").

BIO also remains concerned that additional categories or classes are necessary to account for therapies that do not clearly fall within the existing classifications. Accordingly, we renew our request that the USP address combination therapies such as combination hyptertensive agents, antineoplastic agents, and HIV/AIDS combination products. BIO questions

how the USP determined that a combination product demonstrated an "exclusive clinical benefit" warranting inclusion. What resources did the USP use to determine "clinical benefit," which products were excluded from this list and why, and why is USP using this concept at all? The USP's role is to categorize therapies, not to determine "exclusive clinical benefit."

To the extent that the USP has decided to provide additional guidance in the form of FKDTs and the comprehensive listing, we believe that such guidance should continue to be aimed at increasing beneficiary access to prescription drug therapies. This issue is of particular importance given that the total number of categories and classes did not change in the Revised Guidelines. In fact, it seems that one of USP's primary goals in revising the guidelines was to maintain the same number of arbitrary categories/classes, as this number remained the same despite the fact that many innovative therapies and new indications were approved this past year. Because plan sponsors will consider the Model Guidelines in conjunction with the additional guidance, we believe the USP should ensure that there are enough categories, classes and FKDTs for new and existing therapies and also populate the drug list document appropriately. If there are available therapies, all should be listed to avoid potential confusion as to whether your drug list is comprehensive. As we discuss in more detail below, the process for updating will prove critical in this area. The Revised Guidelines only will be effective if the prescription drugs and biologicals available on any particular plan will suit the needs of Medicare beneficiaries, based on current clinical practice.

II. Mechanism for Including Drugs and Biologicals that Are Used to Treat Rare Diseases

BIO renews its support for the creation of a category and appropriate classes for therapies that treat rare diseases and disorders, such as orphan drugs and biologicals. Each rare disease is caused by a unique deficiency or clinical problem. Unlike some other products, orphan drugs and biologicals are inherently not interchangeable with other therapies. Accordingly, we urge the USP to support drugs and biologicals that treat rare diseases and their broad inclusion in formularies.

Toward that end, we recommend creating a new category or additional classes to ensure that therapies that treat rare diseases are included. Indeed, many of these therapies do not necessarily fall into obvious categories, and those that do run the risk that they will not be

covered, particularly if there are more than two therapies in the same category. For example, the "Enzyme Replacements/Modifiers" therapeutic category, which covers some--but not all orphan drugs--continues not to have any classes or subdivisions within the category. As we emphasized in our comments to the draft Model Guidelines, there should be subcategories or classes to reflect the fact that each disease in the Enzyme Replacements/Modifiers category is a rare disease caused by a unique deficiency or problem and that treatments are not interchangeable among patients with different diseases. Medicare beneficiaries with rare diseases run the risk of having their particular therapy excluded if plans are permitted to have just two drugs for this category or class. We are concerned that this situation will prevent beneficiaries from getting access to the product that addresses their unique clinical problem (*e.g.*, Gaucher's disease, Fabry's disease, MPS I, alpha-1-antitrypsin deficiency). In addition, we are troubled that decisions by the USP may have long-term effects, such as creating significant disincentives to conduct research on drugs and biologicals used to treat rare disorders.

BIO is concerned that even when an appropriate category exists, the Revised Guidelines will continue to fail to protect patients suffering from rare diseases and disorders. We believe that these therapies warrant special consideration given that the loss of access to orphan drugs and biologicals could prove disastrous because these drugs and biologicals often are the only viable therapy for Medicare beneficiaries. Patients with one rare disorder should not be in competition with patients with another rare disorder with regard to coverage under the Model Guidelines. It is not unusual to include and cover a large number of drugs and an entire class for certain diseases. Indeed, CMS has stated in its final formulary guidance for 2006 that it expects that best practice formularies should contain a majority of drugs that are used to treat certain conditions, such as antidepressives, HIV/AIDS, immunosuppressants, anticonvulsants, cancer, and antipsychotics. We believe that orphan drugs and biologicals should be treated similarly, and the USP should include in its Revised Guidelines all or substantially all of the therapies that treat rare diseases. We look forward to working with the USP to achieve this goal.

III. USP Should Identify a Process for Updating the Model Guidelines and Also Release Information Underlying the Model Guidelines

BIO recognizes that the Model Guidelines will need constant monitoring and updating. Indeed, this has been mandated by Congress.[1] We noted in our previous comments on the draft Model Guidelines that there needs to be more predictability and transparency with regard to this process. Specifically, the USP should update the model guidelines at least quarterly to reflect current clinical standards of care. Annual updates are not sufficient. Medicare beneficiaries cannot afford to wait that long to access new and innovative therapies. In particular, there needs to be an immediate process to assess whether a new category or class needs to be established for newly-approved treatments, because of a new indication for an approved therapy, or due to changes in clinical practice. Accordingly, we urge the USP to update the Model Guidelines quarterly and to make these determinations available to the public through its web site.

With regard to the process of updating the Model Guidelines, BIO urges the USP to provide further information on its methodology with regard to the Revised Guidelines. We are unclear as to the details of the USP's process and believe that additional explanation is needed. In particular, BIO requests that the USP provide more information about the criteria that it lists in the Preamble to the Revised Guidelines, and that it define terms such as "clinically distinct" and "clinically non-distinct." Because changes to the Model Guidelines have been made on this basis, we would appreciate a better understanding of how the classification scheme and therapies were evaluated and determined (*e.g.*, What evidence was used or reviewed in making a determination that a product was clinically non-distinct?). This issue is of particular concern for new agents that have recently been or will be approved. We believe that the USP should provide information about what it has examined and considered (*e.g.*, data describing mechanism of action, drug compendia monographs, medical journals, etc.) in reviewing drugs and biologicals that have been newly approved or have new indications, as well as the USP's rationale for determining a new therapy's therapeutic category, pharmacologic class, or new classification, or for not including a particular therapy.

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[1] SSA § 1860D-4(b)(3)(C)(ii).

IV. Conclusion

BIO appreciates this opportunity to comment on the Revised Guidelines. We look forward to continuing to work with the USP and CMS in revising and refining the Model Guidelines to ensure that Medicare beneficiaries have access to the critical drugs and biologicals they need. 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