September 17, 2004

BY HAND DELIVERY

Lynn Lang
United States Pharmacopeia
12601 Twinbrook Parkway
Rockville, MD 20852-1790

Re: Comments to the Draft Model Guidelines by the Biotechnology Industry Organization

Dear Ms. Lang:

The Biotechnology Industry Organization ("BIO") appreciates the opportunity to comment on the United States Pharmacopeia's ("USP") draft Medicare Prescription Drug Benefit Model Guidelines ("Draft Guidelines") that recently were released. BIO is the largest trade organization to serve and represent the biotechnology industry in the United States and worldwide. BIO represents more than 1,000 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. We support the comments to the Draft Guidelines by our various members. BIO writes separately, however, regarding specific concerns to us as an industry organization.

BIO applauds the significant time and effort that the USP and individual members of the Expert Committee have devoted to developing the Draft Guidelines. We recognize the difficulty in assessing the vast amount of clinical

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information available regarding prescription drugs and biologicals and creating therapeutic categories and classes. BIO believes that, if done properly, the development of final guidelines ("Model Guidelines") will be an important component to the new Medicare prescription drug program ("Medicare Part D").

After careful consideration and review of the Draft Guidelines, however, BIO is very concerned that the Model Guidelines will not fulfill the statutory directive of Congress. We 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. Toward that end, BIO recommends (i) that the USP fulfill its charge by Congress to ensure that categories and classes do not provide a means for plans to discourage enrollment of select Medicare beneficiaries; (ii) that the formulary classes and categories be expanded to incorporate the recommended subdivisions listed in the Draft Guidelines, as a first step; (iii) that new categories or classes be created for the clinically important therapies that do not fall within any existing categories and classes; (iv) that a mechanism be created for incorporating drugs and biologicals that are used to treat rare diseases that are not otherwise included in existing classes and categories; and (v) that the USP release information and identify a process for updating the Model Guidelines frequently and with public input, to ensure that beneficiaries have access to new therapies and existing therapies with new indications.

BIO also recognizes the need for changes to classes and categories for clinical reasons, about which its members will comment separately. BIO hopes that the USP will take into consideration these specific comments as it finalizes the guidelines.

BACKGROUND

The addition of the Medicare prescription drug program holds the potential to improve Medicare beneficiaries' access to prescription drugs and biologicals that are not currently covered by Medicare. BIO believes that increased access to prescription therapies will improve the overall health of Medicare beneficiaries. Such an improvement will not be realized, however, if the Medicare Part D prescription drug plans ("PDPs" or "plans") are deficient of available prescription drugs and biologicals. In other words, this new benefit will be compromised unless the Part D program is implemented in a way that causes

PDP formularies to include an adequate number of drugs and biologicals to serve the unique Medicare population. Indeed, Congress was concerned that Part D plans offer a sufficient range of therapies. Specifically, the statute prohibits the approval of a plan that is found to have a design and benefit structure that is "likely to substantially discourage enrollment by certain Part D eligible individuals under the plan."[1]

Simultaneously, Congress directed the Centers for Medicare & Medicaid Services ("CMS" or the "agency") to seek the assistance from the USP in the development of a list of categories and classes (*e.g.*, Model Guidelines) that may be used by PDPs.[2] If a plan's formulary contains categories and classes consistent with the Model Guidelines, CMS may not find that the plan's category and class structure is likely to discourage enrollment by certain beneficiaries. As such, Congress assigned the USP a tremendous responsibility in pursuit of this objective. In addition, the Model Guidelines are important because they may be used as a starting point for formularies developed by private plans.

DISCUSSION

BIO has carefully reviewed the Draft Guidelines, and there are number of issues of concern that we have identified. As noted above, the statute mandates that CMS may not review the formulary categories and classes of plans adopting the Model Guidelines. BIO strongly believes that this requires the USP, in its creation of the categories and classes in the Model Guidelines, to focus on ensuring that there is sufficient access to a wide range of therapies. BIO finds that the USP has not fulfilled its charge and that the Draft Guidelines fall short of this goal. Accordingly, we urge the USP to finalize the Guidelines in a way that closes the numerous gaps that plans would not have to fill under the existing proposed classes and categories. As discussed in greater detail below, BIO recommends that these categories and classes be expanded in a number of ways so that the prescription drugs and biologicals available on any particular plan will suit the needs of Medicare beneficiaries, based on current clinical practice. Finally, BIO

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[1] Social Security Act ("SSA") § 1860D-11(e)(2)(D)(i).

[2] Id. at § 1860D-3(b)(3)(C)(ii).

urges the USP to identify how it will update the Model Guidelines and release the information that underlies the guidelines.

I. The USP Has Not Considered the Unique Nature of the Medicare Population

BIO believes that it is important to remember that the Medicare population that will enroll in the Part D program and benefit from the protections these Model Guidelines will afford is unique. Medicare is a government sponsored program for the elderly, the disabled, and those with end-stage renal disease, and must take into account all beneficiaries. Given that the Medicare population typically has chronic diseases such as cardiovascular disease, osteoporosis, diabetes, chronic pain, or depression, these individuals often require multiple medications over a long period of time. As such, Medicare beneficiaries should not have their health care needs compromised due to inadequate access to needed therapies. BIO is concerned that insufficient consideration has been given by the USP of the distinct needs of this population. In developing the Draft Guidelines, the USP relied heavily on the "environmental scan," which primarily focused on private health insurance plans. BIO is concerned that this reliance does not adequately take into account the Medicare population. Accordingly, when finalizing the guidelines and later modifying them, the USP should focus on the unique needs of the Medicare population.

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

Given that the Model Guidelines will afford some protection from CMS review for PDPs if their formulary classes and categories are consistent, the USP has a significant responsibility to fulfill. Although consistency with the Model Guidelines does not fully insulate a plan from review by CMS, an inadequate category and class structure could have a negative effect on patient access to therapies. As such, BIO strongly believes that the USP's focus in developing 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 is disappointed to find that the USP, in its development of the Draft Guidelines, has attempted to balance the number of categories and classes with the position of the plans that fewer categories and classes are needed to give them flexibility in their formulary design. In particular, the USP indicates that the "Expert Committee has addressed the need to balance patient access with drug plan practicality."[3] BIO believes this focus is misguided and is inconsistent with the USP's charge. Instead, the USP's mandate is to create Model Guidelines that will ensure that plans with formulary classes and categories consistent with them will not discourage plan enrollment. In effect, the inappropriate focus on balancing the desires of plans has resulted in an overly broad set of classes and categories that would allow plans to evade review of whether their formulary structure discourages beneficiaries from enrolling without ensuring that they do. The Draft Guidelines thus must be revised so that plans cannot exclude a large number of critical drugs and biologicals for the Medicare population – a population that relies heavily on these treatments. Although the burden may be greater on the plans to establish formulary classes and categories consistent with the guidelines, PDPs have the option of adopting different categories and classes and having them reviewed by CMS. Ultimately, any balancing of the need for plan flexibility should be left up to CMS in implementing the new prescription drug program, not to the USP.

BIO urges the USP to fulfill its statutory responsibilities by modifying the Draft Guidelines to ensure greater access to important drugs and biologicals under the Part D benefit and to prevent plans from evading their responsibilities under the Medicare prescription drug program. We make specific recommendations for achieving this goal below.

III. Comments Regarding Current Classes and Categories

BIO urges the USP to ensure that the Model Guidelines serve the purpose that Congress intended by providing a comprehensive matrix of categories and classes so that Medicare beneficiaries are not denied the therapies they need. Based on our review of the Draft Guidelines, we recommend a number of changes, centering around increasing the granularity of the classes and categories.

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[3] See "Summary of USP Approach and Methodology to Draft Model Guidelines," p. 11, August 2004, available at http://www.usp.org/drugInformation/mmg/draftmodelGuidelines.html.

A. Include All Recommended Subdivisions as Classes and Categories

BIO applauds the USP's decision to add an additional level of granularity in a third column of the Draft Guidelines. These recommended subdivisions exemplify that many of the existing categories and classes have a variety of drugs and biologicals that can be further subdivided based on mechanism of action and indication. In the absence of such subdivisions, the rather broad categories and classes eliminate a host of therapies. Nonetheless, we are disappointed that these groupings are identified as "subdivisions" rather than classes or categories (which are subject to a two drug or biological minimum). Accordingly, BIO urges the USP to include all of the recommended subdivisions in the Draft Guidelines as classes in the final guidelines. This will be a helpful first step in ensuring that additional therapies are available to beneficiaries, although we note that revisions to the identified categories, classes, and subdivisions may be warranted.

B. Antineoplastics

BIO is particularly concerned that the therapeutic category of antineoplastics has been subdivided only into nine general pharmacologic classes, with two subdivisions. Cancer treatment is complex, and the types of agents used continue to evolve. Unlike other therapeutic categories, antineoplastics may be used for more than one organ system, for more than one type of cancer, for different stages of diseases, and often in combination with other agents. More critical, unlike other treatments that may be interchangeable in treating various diseases and disorders, cancer therapy does not have the same level of flexibility. BIO urges the USP to reexamine the categories, classes, and subdivisions for antineoplastics to take into account the complexity of cancer treatment and therapy. As it stands, even if the subdivisions in the Draft Guidelines became classes or categories, plans only would be required to offer a minimal number of oncology therapies to be compliant with the guidelines. Medicare beneficiaries battling cancer cannot afford to have their access to antineoplastics limited this severely.

C. Vaccines

BIO recognizes that certain vaccines are covered under Medicare Part B and is pleased that the Part D program will provide "wrap around" coverage of additional vaccines for Medicare beneficiaries. We note, however, that the Draft Guidelines defeat this purpose. Indeed, vaccines are included in the Draft Guidelines only as a recommended subdivision under the general "Immune Stimulant" class that also includes toxoids and other immune stimulants and as a class under the "Antivirals" therapeutic category. BIO finds this placement insufficient, even if the subdivisions in the Draft Guidelines became classes or categories. Indeed, a plan that creates classes and categories consistent with the Draft Guidelines would avoid full scrutiny despite the fact the plan provided no vaccines to Medicare beneficiaries. If the vaccine subdivision were to become a category or class, access would be insufficient, as a plan could only provide two vaccines and meet the guideline standard without regard to the range of ailments for which vaccines are warranted.

BIO's members are developing a host of vaccines that target a variety of diseases in the aged and disabled Medicare populations. We believe that these vaccines will provide added wellness benefits to beneficiaries and in the long term, will prove to have added cost-benefits. We recommend that the USP correct this deficiency by making a sufficiently diverse set of categories or classes to accommodate a meaningful range of vaccines, particularly for the elderly, dual-eligible, and immunosuppressed populations of beneficiaries who require such access.

D. Creating Categories or Classes for Products That Have Been Overlooked and Enhancing Specific Categories/Classes

BIO is disheartened to see that the USP seemingly has overlooked a number of therapies in the Draft Guidelines and has decreased the chances that certain types of treatments will be selected by drawing broad categories and classes. Although we are pleased that the USP has taken steps to identify the major categories and classes, we believe that the Draft Guidelines do not adequately account where all therapies in a given area will map. Because CMS requires, at a minimum, only two therapies for each category and class, the Model

Guidelines should have enough granularity so that beneficiaries do not run the risk of losing access to the therapies they need most. More important, BIO recommends that the USP ensure that each drug and biological *conceivably* may be placed in at least one of the categories or classes in the Model Guidelines. Beneficiaries should not lose access to a particular therapy simply because there was no specific class or category available. For example, the Draft Guidelines do not appear to provide an adequate category or class for all types of phosphate binders, which are required by end stage renal disease ("ESRD") beneficiaries. Given that all ESRD patients are covered by Medicare, regardless of age, it is particularly imperative that these beneficiaries are not deprived of needed therapies. As such, the USP should be more comprehensive to further distinguish the differences among drugs and biologicals, so that appropriate classes and categories are drawn.

Second, BIO is concerned how certain therapies, or combinations of therapies, that are not easily classified or categorized, are treated under the Draft Guidelines. In particular, BIO recommends that the USP take special consideration of diseases or conditions that require a variety of therapies that may fall in numerous categories. For example, multiple sclerosis ("MS") has a variety of treatments (*e.g.*, immunomodulators, immunosuppressants) that could fall into a number of categories and classes (or none at all) in the Draft Guidelines. Medicare beneficiaries, such as those with MS, will effectively be denied access if only part of their therapeutic regimens are available. As we emphasize here and in other parts of these comments, BIO urges the USP to make the Draft Guidelines more granular, so that the purpose of the Model Guidelines will not be undermined.

E. Mechanism for Including Drugs and Biologicals That Are Used to Treat Rare Diseases

As we have highlighted in a few examples above, BIO believes the categories and classes under the Draft Guidelines are insufficient. Of particular concern is that certain therapies used to treat rare diseases and disorders (*e.g.*, Idiopathic Pulmonary Fibrosis), such as orphan drugs and biologicals, will fall out of the reach of beneficiaries. Indeed, many of these therapies do not necessarily fall into obvious categories, and those that do (*e.g.*, "Enzyme Replacements/ Modifiers") 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 does not have any classes or subdivisions within the category. There should be subcategories or classes to reflect the fact that each disease in this category is a rare disease caused by a unique deficiency or problem, and therefore, are not interchangeable among patients with different diseases (*e.g.*, Gaucher's disease, Fabry's disease, MPS I, alpha-1-antitrypsin deficiency). Allowing plans to have just two drugs per category or class will preclude other beneficiaries with rare diseases from getting access to the product that addresses their unique enzyme problem. The loss of access to these treatments by beneficiaries would prove disastrous, particularly in the case of orphan drugs and biologicals, as these therapies often are the only viable therapy for Medicare beneficiaries. These therapies warrant special consideration, because, unlike other therapeutic categories, these treatments are not interchangeable. BIO believes that patients with one rare disorder should not be in competition with patients with another rare disorder with regard to coverage under the Model Guidelines. As such, BIO strongly urges the USP to give thoughtful consideration to these therapies, in particular orphan therapies, and to develop a mechanism for including drugs and biologicals that are used to treat rare disorders and diseases.[4] We look forward to working with the USP to achieve this goal.

Apart from the recommendations we make specifically about the Draft Guidelines, it is important to note that there may be indirect consequences of inadequate Model Guidelines. BIO represents an industry that is devoted to discovering new cures and therapies that primarily affect the disabled and elderly, and the biotechnology industry is particularly sensitive to changes in the Medicare program. We hope that the Model Guidelines will not deter the industry from developing further innovations by severely limiting beneficiary access to these unique and lifesaving therapies.

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[4] We recognize that "rare disorder or disease" goes more to symptoms and diseases and less to particular mechanisms of action for a particular therapy. BIO seeks to work with the USP to develop a meaningful definition (*e.g.*, as defined by the National Institutes of Health) or other criteria for the Model Guidelines (*e.g.*, include those drugs with orphan approval), so that beneficiaries will have full access to these lifesaving therapies.

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

BIO, like Congress,[5] recognizes that the Model Guidelines that the USP releases later this year will need constant monitoring and updating. The USP has failed to provide any detail on its process for updating the Model Guidelines and instead, has offered only passing mention of this duty and its specific plans. As such, BIO recommends that the USP detail the processes and criteria it will use to update the Model Guidelines. 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. Moreover, the USP should assess, on a quarterly basis, whether a new class or category is required because of a new indication for an approved therapy or due to changes in clinical practice and make these determinations available to the public (*e.g.*, through its web site).

Finally, BIO requests that the USP provide a list of all Food and Drug Administration approved therapies and their assigned categories and classes, as directed by the cooperative agreement.[6] BIO is disappointed that the USP has not already released this listing along with the Draft Guidelines to facilitate the public's review. We believe this information will aid the public's continued assessment of the Model Guidelines and will satisfy the USP's stated commitment to keep the process open and transparent to the public. Further, BIO recommends that the USP release the background database so that the public has more information about the decision-making processes underlying the development of the Draft Guidelines. BIO urges the USP to release this information expeditiously.

CONCLUSION

BIO appreciates the opportunity to comment on the Draft Guidelines and applauds the USP on its efforts thus far. We look forward to the opportunity of working with the USP and the agency to develop Model Guidelines that allow for clinically appropriate combination therapies, provide Medicare beneficiaries

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[5] SSA § 1860D-4(b)(3)(C)(ii) (requiring the guidelines to be revised from time to time).

[6] See "USP Statement on Draft Model Guidelines," (Aug. 20, 2004).

with adequate and real choices, and expand access to drugs and biologicals under Medicare that have not been available until now.

Respectfully submitted,

/s/

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Chief of Policy