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November 15, 2004

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Dear Ms. Brill and Ms. Hayes:

The Biotechnology Industry Organization ("BIO") appreciates this opportunity to comment on the Proposed Guide to Vermont's Pharmaceutical Marketer Price Disclosure Law<sup>1</sup> (the "Proposed Guide"). 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.

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<sup>1</sup> 33 V.S.A. § 2005a.

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BIO appreciates the Attorney General's office's efforts to provide guidance to affected pharmaceutical manufacturers and biotechnology companies on Vermont's Pharmaceutical Marketer Price Disclosure Law. We are concerned, however, that the Proposed Guide poses significant practical challenges for pharmaceutical manufacturers and biotechnology companies and that the resulting information reported to prescribers may not be meaningful. In particular, BIO believes that the Proposed Guide's proposal for comparing prices among therapies that are available in forms other than pills will not provide a useful comparison for prescribers. In addition, BIO is concerned that the Proposed Guide relies on the proposed therapeutic categories developed by the United States Pharmacopeia ("USP"), published in the "Medicare Prescription Drug Benefit Draft Model Guidelines: Drug Categories and Classes in Part D" (the "USP Draft Model Guidelines"). These USP Draft Model Guidelines contain significant flaws and will not provide a meaningful comparison of prices for prescribers. Finally, we are concerned that the requirements of the Vermont law will subject pharmaceutical manufacturers and biotechnology companies to potentially conflicting state and federal regulatory and legal duties. We have addressed each of these concerns in greater detail below.

I. Required Disclosures – "Per Pill" Comparisons

Section 4 of the Proposed Guide sets forth the specific disclosure requirements for affected pharmaceutical manufacturers and biotechnology companies. These include a requirement that manufacturers report the Average Wholesale Price ("AWP")<sup>2</sup> per pill of the manufacturer's drugs and biologicals as well as the price relationship between the drug or biological being marketed and other drugs or biologicals within the same therapeutic class. If either the drug or biological being marketed or the other therapies in the same class are in liquid, aerosol, or other non-pill form, then manufacturers must disclose the AWP based upon daily dosage and 30-day (or acute) course of therapy. The Proposed Guide

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<sup>2</sup> We note that this term is used in the statute as though it were established by the pharmaceutical manufacturers and biotechnology companies and represents the actual price at which drugs and biologicals are sold to wholesalers. This is not the case, in our experience.

requests comments on whether requiring the disclosure of prices for drugs and biologicals that are not in pill form is feasible and advisable.

BIO believes that it is neither feasible nor advisable to compare the AWP of therapies that are not available in pill form. Biological therapies include therapies that must be injected, infused, or inhaled. Because of these unique and variable administration forms, it would be extremely difficult to determine a "per pill" or "per 30 days" price for these therapies. The dosage for these types of therapies does not translate into "per day" or "per 30 day" treatment classifications. Providing prescribers with information on these therapies based on such comparisons will only serve to confuse rather than inform prescribers. The statute clearly contemplates that manufacturer disclosure "shall include the AWP per pill"<sup>3</sup> but makes no provision for the disclosure of other forms of prescription therapies.

Not only is it not feasible to determine a "per 30 day" price for many biological therapies, it is not appropriate to compare biological therapies that may fall in the same therapeutic class. Injectables in the same class may have very different dosages, and any effort to evaluate these therapies on a "per day" basis would fail to take into account the variety of doses and the frequencies of administration that exist across individual indications and patient populations within each product class. For example, a range of chemotherapy treatments may be prescribed for therapy regimens of different doses and duration. Dosing will depend on the type of cancer being treated, the length and frequency of the course of therapy, and the patient's individual physiological responses to the therapy. Depending on the type and duration of therapy, the level of supportive care needed for a patient may vary. As a result, price comparisons of therapies within classes of injectables would be essentially meaningless, because such comparisons would tell prescribers very little about the costs of an individual patient's treatment.

Furthermore, many biological therapies are administered in a physician's office. Most drugs and biologicals administered in a physician's office are purchased by the physician, and the physician will be well aware of the acquisition cost for the therapies purchased for administration in the office. Similarly, injectable therapies administered in the hospital setting are generally reimbursed pursuant to the DRG system, making price irrelevant to prescribers.

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<sup>3</sup> 33 V.S.A. § 2005a(a).

Rather, price is generally monitored through hospital formularies. Requiring pharmaceutical manufacturers and biotechnology companies to provide the AWP in these circumstances will not assist the prescriber in providing cost effective therapies to patients. We urge the Attorney General's office to exclude drugs and biologicals administered in non-pill form from coverage under the Proposed Guide. This would be consistent with the statute, as well as with federal policy.

## II. Proposed Use of USP Categories and Classes

The Proposed Guide requires manufacturers to provide the AWP per pill of other drugs and biologicals in the same therapeutic class. The Proposed Guide defines "therapeutic class" as the 146 therapeutic categories and pharmacologic classes defined in the USP Draft Model Guidelines. BIO believes that the use of the USP Draft Model Guidelines is, at best, premature. Below we have detailed some of the problems posed by reliance on the USP Draft Model Guidelines.

The USP Draft Model Guidelines initially were published in August of 2004 and are still in draft form. During the public comment period, the USP received over 1100 comments, and the USP currently is working to revise the categories and classes. The USP is expected to submit final Model Guidelines to the Centers for Medicare and Medicaid Services ("CMS") by the end of December and is not expected to issue final Model Guidelines to the public for several months. We are hopeful that the USP ultimately will design categories and classes that provide meaningful therapeutic comparisons. In the meantime, the USP Draft Model Guidelines represent simply a draft document that does not provide for appropriate comparisons of drugs and biologicals. Relying on this draft for imposing price reporting requirements on pharmaceutical manufacturers and biotechnology companies will result in an unwieldy and impractical disclosure system that will not provide physicians and other prescribers with meaningful price comparisons.

The USP Draft Model Guidelines and Vermont's Proposed Guide were developed for very different purposes. The Proposed Guide is designed to implement the reporting requirements under the Vermont's Pharmaceutical Marketer Price Disclosure law, requiring certain manufacturers to disclose prescription drug prices to Vermont physicians and other prescribers. The USP

Draft Model Guidelines, on the other hand, are designed to establish minimum formulary standards under the Medicare prescription drug benefit, enacted by the Medicare Prescription Drug Improvement and Modernization Act of 2003 (the "MMA"). Congress enacted the new Medicare prescription drug benefit as a means of improving Medicare beneficiaries' access to prescription drugs and biologicals that are not currently covered by Medicare. Under this new Medicare benefit, prescription drug plans ("PDPs") will offer senior citizens access to a prescription drug benefit. In the MMA, Congress directed the Centers for Medicare and Medicaid Services ("CMS") to seek assistance from the USP in developing a list of categories and classes of prescription drugs that would be used to establish minimum standards for PDPs that choose to use formularies in designing their Medicare prescription drug programs.

BIO is concerned that the therapeutic categories and classes set forth in the USP Draft Model Guidelines are too broad for purposes of the Medicare prescription drug benefit. The overbroad nature of this classification system also presents problems for manufacturers attempting to comply with Vermont's Proposed Guide.

For example, the USP Draft Model Guidelines include the therapeutic category of antineoplastics, subdivided into only nine pharmacologic classes, with two subdivisions. This categorization does not adequately reflect the complex nature of cancer treatment. 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 importantly, unlike other treatments that may be interchangeable in treating various diseases and disorders, cancer treatment often does not have the same level of flexibility. Under the Proposed Guide, pharmaceutical manufacturers and biotechnology companies will be required to provide pricing information for physicians on a wide range of cancer therapies that may be used in a number of different dosages and for different diseases. Because appropriate dosing is widely variable, this information is likely to be difficult for manufacturers to report in a manner that provides useful information to prescribers. In fact, the result is likely to be that prescribers receive volumes of information that render the underlying goal of the Vermont statute somewhat meaningless.

Similarly, under the USP Draft Model Guidelines, drugs and biologicals used to treat rare diseases and disorders, such as orphan drugs and biologicals, tend to be lumped together in a class with multiple other therapies.

For example, "Enzyme Replacements/Modifiers" is a category under the USP Draft Model Guidelines. Yet each disease in this category is a rare disease caused by a unique deficiency or problem – such as Gaucher's disease and Fabry's disease – and therefore, therapies in this category are not interchangeable among patients with different diseases. As another example, the USP Draft Model Guidelines also include all vaccines in a single class. Thus, a biotechnology company that markets a vaccine for influenza to a Vermont physician would be required to provide that physician with the AWP for all vaccines included in the USP class. Providing the physician with the AWP for an anthrax vaccine when marketing a flu vaccine will not assist that physician in providing his or her patients with cost-effective therapies. In both of these examples, providing prescribers with pricing information on all of the drugs and biologicals within the USP category will result in the prescriber receiving substantial quantities of irrelevant information, potentially having a detrimental impact on patient care.

Because the USP categories and classes are inadequate from a clinical standpoint, reliance on the USP Draft Model Guidelines will result in prescribers receiving information that is meaningless for purposes of providing their patients with price comparisons of similar therapies. We urge the Vermont Attorney General's office to eliminate the Draft Guidance's reliance on the USP Draft Model Guidelines.

### III. Potential Conflict with Federal Law

Although the Proposed Guide attempts to implement the new Vermont Pharmaceutical Marketer Price Disclosure Law, we are concerned that both the Law and any attempt to implement it could create a conflict between the Law and the Federal Food, Drug and Cosmetic Act ("FDCA") and implementing regulations promulgated by the United States Food and Drug Administration ("FDA").

Section 502 of the FDCA<sup>4</sup> establishes the standard for drug misbranding. Under this authority, FDA has promulgated regulations prohibiting as misleading certain comparative claims in advertisements for prescription drugs.<sup>5</sup> FDA has further interpreted the regulation as prohibiting many comparative claims

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<sup>4</sup> 21 U.S.C. § 352.

<sup>5</sup> See 21 CFR 202.1(e)(6)(ii).

of cost effectiveness and pharmacoeconomic benefit.<sup>6</sup> The agency has expressed particular concern regarding the oversimplification and misleading nature of price and cost comparisons that inappropriately imply that referenced drugs have comparable clinical benefit and fail to take into consideration issues such as variation in dosage requirements, increased possibility of adverse events, frequency of laboratory tests required, and the need for additional medication that may affect the overall cost effectiveness of the drug.<sup>7</sup> With regard to pricing information, FDA has argued that to comply with the regulations, advertisers must identify the source of the data included in promotional material and disclose its limitations.<sup>8</sup> For example, advertisements including average wholesale price (“AWP”) must disclose that the figure may not reflect the final prices paid by pharmacies or consumers.<sup>9</sup>

Although federal law does allow drug and biologics manufacturers to include certain economic information in promotional material, the scope of that permission is narrow. For example, health care economic information provided to a formulary committee or similar organization shall not be deemed false or misleading if it pertains to an approved use.<sup>10</sup> And, pricing information provided in drug reminder advertisements may be exempt from the prohibition on comparison claims.<sup>11</sup> Reminder advertisements, however, constitute only a small number of the drug labeling materials falling within the scope of the Vermont law.<sup>12</sup>

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<sup>6</sup> See generally Regulatory Letter from FDA to Janssen Pharmaceutica (March 30, 2000); Warning Letter from FDA to Novartis Pharmaceuticals Corporation (January 21, 1999); Warning Letter from FDA to Unimed Pharmaceuticals, Inc. (September 1, 1999); Regulatory Letter from FDA to Oclassen Pharmaceuticals, Inc. (April 28, 1998); Warning Letter from FDA to Eli Lilly and Company (July 19, 1994)

<sup>7</sup> See, e.g., Regulatory Letter from FDA to Janssen Pharmaceutica (March 30, 2000); Warning Letter from FDA to Unimed Pharmaceuticals, Inc. (September 1, 1999); Warning Letter from FDA to Novartis Pharmaceuticals Corporation (January 21, 1999).

<sup>8</sup> See, e.g., Regulatory Letter from FDA to Janssen Pharmaceutica (March 30, 2000); Regulatory Letter from FDA to Fujisawa Healthcare, Inc. (November 29, 1999); Warning Letter from FDA to Novartis Pharmaceuticals Corporation (January 21, 1999); Warning Letter from FDA to Eli Lilly and Company (July 19, 1994).

<sup>9</sup> See, e.g., Warning Letter from FDA to Watson Pharmaceuticals, Inc. (December 22, 1998); Regulatory Letter from FDA to Oclassen Pharmaceuticals, Inc. (April 28, 1998); Warning Letter from FDA to Eli Lilly and Company (July 19, 1994).

<sup>10</sup> See Food and Drug Administration Modernization Act of 1997, P.L. 105-115, Sec. 114(a) (*amending* 21 U.S.C. 352(a)).

<sup>11</sup> 21 C.F.R. 200.200(a).

<sup>12</sup> *Id.* 202.1(e)(2)(i).

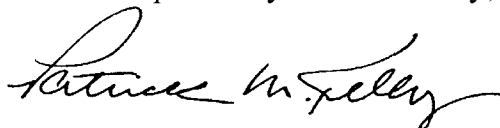
Ms. Brill and Ms. Hayes  
Vermont Attorney General's Office  
November 15, 2004  
Page 8 of 8

Consequently, BIO is concerned that implementation of the Vermont law will subject drug and biologics manufacturers to potentially conflicting regulatory and legal duties.<sup>13</sup> Therefore, we urge that Vermont proceed carefully and only after a thorough analysis of federal requirements governing drug labeling and advertising.

Finally, in Section 6, the draft guide details disclaimers for all disclosures required by the Vermont law. In our view, no state disclaimer could release a pharmaceutical manufacturer or biotechnology company from the prohibitions in the FDCA noted above.

Thank you for your consideration of these comments. We would welcome the opportunity to discuss these issues in depth. Please contact India Valentine at (202) 962-9514 if you have any questions regarding our comments.

Respectfully submitted by,



Patrick M. Kelly  
Vice President  
State Government Relations

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<sup>13</sup> See *Hurley v. Lederle Labs*, 863 F.2d 1173, 1179-80 (5<sup>th</sup> Cir. 1988). See also U.S. Amicus Brief in Support of Defendant-Appellee and Cross-Appellant, *Motus v. Pfizer, Inc.*, No. 55498 (9<sup>th</sup> Cir. Filed Sept. 3, 2002); U.S. Statement of Interest, *In re Paxil Litigation*, Civ. No. 01-07937 (C.D. Cal. Filed Sept. 4, 2002).