

February 13, 2002

Dockets Management Branch
Food and Drug Administration
Room 1-23
12420 Parklawn Drive
Rockville, Maryland 20857

Re: Docket No. 01P-0586 – Comments of GPhA

Dear Food and Drug Administration:

The Generic Pharmaceutical Association applauds FDA's recent decisions to approve a number of generic versions of Bristol-Myers Squibb Company's Glucophage® (metformin hydrochloride). Those approval decisions, coming just a short time after the Best Pharmaceuticals for Children Act became federal law, properly implemented the intent of Congress that generic drug products should be approved – expeditiously and without unnecessary administrative proceedings – with the omission of exclusivity-protected pediatric use labeling information. FDA's approval decisions benefit taxpayers, third party payors, and consumers, who finally have access to lower cost generic versions of Glucophage, an important drug product.

GPhA is submitting, for the record, its detailed response to the December 26, 2001 citizen petition filed on behalf of Bristol-Myers. While the Bristol-Myers petition has been rendered moot by FDA's recent approval decisions, we hope that the views set forth in our comment will help pave

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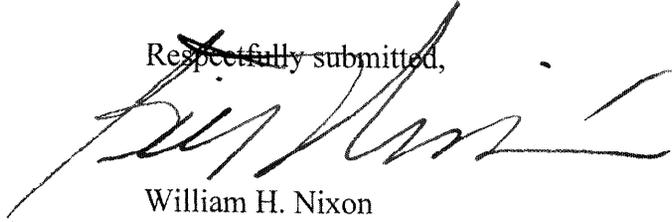
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the way for prompt FDA approvals of other generic drug products, without exclusivity-protected labeling information.

GPhA appreciates this opportunity to express its views.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "William H. Nixon", written over the typed name below.

William H. Nixon
President and CEO

Enclosure

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Food and Drug Administration
Room 1-23
12420 Parklawn Drive
Rockville, Maryland 20857

Re: Docket No. 01P-0586 – Comments of GPhA

Dear Food and Drug Administration:

These comments of the Generic Pharmaceutical Association (GPhA) are respectfully submitted in opposition to the December 26, 2001 citizen petition filed on behalf of Bristol-Myers Squibb Company (Bristol-Myers) by its counsel. For the reasons discussed below, Bristol-Myers' citizen petition is nothing more than a meritless, last ditch effort to block generic competition for its Glucophage®, as well as generic versions of other important innovator drug products. Bristol-Myers' petition is fatally flawed, both procedurally and substantively. As a result, it should be denied.

The Bristol-Myers citizen petition was framed in the context of its blockbuster drug Glucophage (metformin hydrochloride), a widely prescribed diabetes medication. A substantial number of GPhA member firms have pending applications for generic versions of Glucophage. Of equal importance, the issues raised by the Bristol-Myers petition extend to all drug products that are, or could be, used in children. Thus, the Bristol-Myers petition raises issues that are of great interest to GPhA and its members.

GPhA is the national, not-for-profit trade association that represents all segments of the U.S. generic pharmaceutical industry. GPhA's members include finished dosage form product manufacturers, active pharmaceutical ingredient suppliers, and suppliers of other goods and services to the U.S. generic pharmaceutical industry. Members run the spectrum from individuals to multinational firms. The lower cost, safe, and effective generic drug products manufactured and distributed by GPhA's members are an integral part of the solution to rising healthcare costs.

I. BRISTOL-MYERS' CITIZEN PETITION SHOULD BE SUMMARILY DENIED BECAUSE IT IS FLAWED PROCEDURALLY.

The Food and Drug Administration's (FDA) regulation on the submission of a citizen petition is clear and unambiguous – if a petition requests the issuance of an order, the “exact wording” requested for the proposed order “must” be provided to FDA. 21 C.F.R. § 10.30(b). While Bristol-Myers contends that FDA should adopt regulations before implementing the Best Pharmaceuticals For Children Act (BPC Act), Bristol-Myers fails to provide any suggested language. A major pharmaceutical firm like Bristol-Myers and its counsel, a major law firm, certainly must be familiar with FDA's regulation on citizen petitions. Yet Bristol-Myers chose not to comply and did not provide FDA with the benefit of its views on specific language for the requested regulations. GPhA can only assume that Bristol-Myers took this approach because its real intent was delaying generic competition, not assisting FDA with implementing the BPC Act.

Because Bristol-Myers failed to comply with FDA's procedures for citizen petitions, FDA should not expend any of its scarce resources in conducting a substantive review of the petition.

Bristol-Myers' citizen petition should be summarily denied without regard to the relief sought or the arguments raised.¹

II. THE RELIEF SOUGHT BY BRISTOL-MYERS SHOULD BE DENIED BECAUSE IT IS WITHOUT ANY MERIT.

A. Background.

The Hatch-Waxman Amendments of 1984 to the Federal Food, Drug, and Cosmetic Act (FDC Act) established the abbreviated new drug application (ANDA) procedure for generic versions of innovator drug products. One of Hatch-Waxman's trade-offs for the innovator drug industry is the availability of three-years of non-patent exclusivity. In relevant part, three years of exclusivity is available in connection with the approval of a supplement to a new drug application (NDA) that provides for additional indications for use, when the supplemental NDA approval is based on reports of new clinical investigations that are essential to the approval. During that 3-year period, FDA cannot approve an ANDA for the change approved in the supplement. 21 U.S.C. § 355(j)(5)(D)(iv); 21 C.F.R. § 314.108.

While the general rule is that an ANDA product must have the "same" labeling as the NDA product upon which it relies, see 21 U.S.C. § 355(j)(2)(A)(v) and 21 C.F.R. § 314.94(a)(8)(iv), the sponsor of an ANDA can omit "an indication or other aspect of labeling protected by patent or accorded exclusivity under [21 U.S.C. § 355(j)(5)(D)]," 21 C.F.R. § 314.94(a)(8)(iv). That FDA interpretation was upheld by the U.S. Court of Appeals for the District of Columbia Circuit in Bristol-Myers Squibb Co. v. Shalala, 91 F.3d 1493 (D.C. Cir. 1996).

¹ A cursory review of the petition would have shown that it does not "appear[] to meet" FDA's procedural requirements for citizen petitions. Thus, FDA could have refused to accept the petition for filing. See 21 C.F.R. § 10.30(c).

Against this background, in December 2001, Congress passed the BPC Act. The legislation was signed into law by the President on January 4, 2002. Pub. L. No. 107-109, 115 Stat. 1408. Relevant provisions of the BPC Act address the arguments of Bristol-Myers and other innovator companies that, despite the FDA regulation and judicial decision discussed above, FDA could not approve an ANDA by omitting an exclusivity-protected pediatric use labeling statement. Of relevance to the Bristol-Myers citizen petition, section 11 of the BPC Act amended the FDC Act to provide:

GENERAL RULE – A drug for which an application has been submitted or approved under [21 U.S.C. § 355(j)] shall not be considered ineligible for approval under that section or misbranded under [21 U.S.C. § 352] on the basis that the labeling of the drug omits a pediatric indication or any other aspect of labeling pertaining to pediatric use when the omitted indication or other aspect is protected by patent or by exclusivity under clause (iii) or (iv) of [21 U.S.C. § 355(j)(5)(D)].

21 U.S.C. § 355a(o)(1).

New 21 U.S.C. § 355a(o)(2) provides that, if a pediatric indication or other pediatric labeling is omitted, FDA “may” require the labeling of the ANDA product to include a statement that the drug is not labeled for pediatric use, or other information FDA considers necessary.

New 21 U.S.C. § 355a(o)(3) provides that the legislation does not affect “the availability or scope of exclusivity under [21 U.S.C. § 355] for pediatric formulations” or “the question of the eligibility for approval of any application under [21 U.S.C. § 355(j)] that omits any other conditions of approval entitled to exclusivity under clause (iii) or (iv) of [21 U.S.C. § 355(j)(5)(D)].”

Section 11(b) of the BPC Act provides that new 21 U.S.C. § 355a(o) is effective upon enactment, and expressly applies to all ANDAs that are approved or pending on the enactment date.

In anticipation of the President's signing of the BPC Act into law, Bristol-Myers on December 26, 2001, through counsel, submitted its citizen petition to FDA. The Bristol-Myers petition contends that FDA should adopt implementing regulations before approving any generic drug products based on new 21 U.S.C. § 355a(o). In particular, Bristol-Myers contends that FDA should adopt a regulatory scheme that includes the following:

- Before approving any ANDA for a drug product for which exclusivity-protected pediatric use labeling would be omitted, FDA should conduct a proceeding to determine relative health and safety risks and whether additional labeling statements regarding pediatric use are necessary.
- For each such ANDA, FDA should determine what labeling information is necessary to protect the NDA sponsor's pediatric exclusivity.
- With respect to these two determinations, FDA should take into account the possibility of off-label usage.

B. Since Section 11 Of The BPC Act Is Self-Executing, FDA Need Not Engage In Any Rulemaking Before Implementing Section 11.

The crux of Bristol-Myers' argument is that section 11 of the BPC Act is not self-executing; therefore, FDA should adopt regulations before it implements section 11. That proposition is without merit.

As noted, section 11 provides that it is effective upon enactment, and applies to all pending and approved ANDAs. There is no reference to implementing regulations (whether required or

merely authorized); in fact, there is not even any reference to the adoption of FDA guidance documents before implementation. The language of section 11 is plain – Congress intended for FDA to implement the new statutory provision immediately, applying it to both pending and approved applications, without engaging in a time-consuming rulemaking proceeding.² FDA does not have the discretion to defer implementation.

The fact that Congress did not require FDA to engage in rulemaking, or even to adopt a guidance document, before implementing new 21 U.S.C. § 355a(o) stands in marked contrast with other provisions of the BPC Act. Section 17(a) of the BPC Act requires FDA to promulgate a final rule within one year of the date of enactment regarding adverse event reporting for approved drug products. Section 3 of the BPC Act requires FDA to issue guidance regarding the process for submitting responses to written requests for pediatric studies, within 270 days after the date of enactment. If Congress wished to tie the implementation of section 11 to an FDA rulemaking or guidance, it clearly knew how to so specify. It is a well-established principle of statutory construction that “[w]here Congress includes particular language in one section of a statute but omits it in another section of the same Act, it is generally presumed that Congress acts intentionally and purposely in the disparate inclusion or exclusion.” Brown v. Gardner, 513 U.S. 115, 120 (1994), quoting Russello v. United States, 464 U.S. 16, 23 (1983).

Bristol-Myers points to the Congressional consideration of the BPC Act, quoting statements by two Members of Congress in an effort to support its position that FDA should adopt regulations

² GPhA does not dispute that FDA can, within its discretion and using its own timetable, conduct a notice and comment rulemaking proceeding regarding implementation of new 21 U.S.C. § 355a(o). That authority exists under FDA’s general authority to promulgate regulations for the efficient

before implementing 21 U.S.C. § 355a(o). It is well recognized by the courts that such statements by individual Members of Congress are entitled to little, if any, weight:

[A] court would be well advised to take with a large grain of salt floor debate and statements placed into the Congressional Record which purport to create an interpretation for the legislation that is before us.

Landgraf v. USI Film Products, 511 U.S. 244, 262 n.15 (1994), citing 137 Cong. Rec. S15325 (Oct. 29, 1991); accord United States v. Hansen, 566 F. Supp. 162, 168 (D.D.C. 1983), citing NLRB v. Fruit and Vegetable Packers and Warehousemen, 377 U.S. 58, 66 (1964).

Bristol-Myers contends that FDA needs to revisit a number of its regulations in light of section 11. GPhA disagrees. As noted, regulation 21 C.F.R. § 314.94(a)(8)(iv) – which was upheld by the D.C. Circuit – clearly permits FDA to approve an ANDA by omitting exclusivity-protected labeling information. That conclusion is reinforced by the BPC Act.

Even if Bristol-Myers is correct that some existing regulations need revision in light of the new 21 U.S.C. § 355a(o), the desirability of eventual rulemaking should not prevent FDA from implementing the new statutory provision immediately, as Congress intended. If FDA believes that an existing regulation is inconsistent with the mandate of new § 355a(o), FDA can – and must – regulate directly from the statute, disregarding the regulation in question. Section 11 does not give FDA the option of doing otherwise. FDA has regulated directly from the statute before, with judicial approval. In response to court decisions involving 180-day generic drug exclusivity (21 U.S.C. § 355(j)(5)(B)(iv)), FDA announced that, pending future rulemaking, it would “regulate directly from the statute, and . . . make decisions . . . on a case-by-case basis.” FDA Guidance for

enforcement of the FDC Act, 21 U.S.C. § 371(a). The important point, however, is that FDA is not

Industry: 180-Day Generic Drug Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act (June 1998), 63 Fed. Reg. 37,890 (July 14, 1998). This approach was upheld by the D.C. Circuit in Purepac Pharmaceutical Co. v. Friedman, 162 F.3d 1201, 1204-05 (D.C. Cir. 1998), and cited with approval in Teva Pharmaceuticals, U.S.A. v. FDA, 182 F.3d 1003, 1005 (D.C. Cir. 1999).

Turning to the specific regulations sought by Bristol-Myers, Bristol Myers envisions that FDA would conduct a “proceeding,” with opportunity for public input, in connection with the possible approval of any generic drug product for which pediatric use labeling information would be omitted pursuant to new 21 U.S.C. § 355a(o). Having to conduct such a “proceeding” in each instance where the omission of exclusivity-protected pediatric use labeling information is sought by an ANDA sponsor would represent an entirely unwarranted use of the agency’s scarce resources. There is no question that having to conduct such a “proceeding” would substantially delay the approval of generic drug products, which would be directly contrary to the intent of the Hatch-Waxman Amendments: “Congress sought to get generic drugs into the hands of patients at reasonable prices – fast.” In re Barr Laboratories, Inc., 930 F.2d 72, 76 (D.C. Cir. 1991). It would effectively tie FDA’s hands and compel a fundamental change in the way in which FDA has made its drug approval decisions – whether for innovator products or generic products – over the years.³ Thus, there should be no doubt that Bristol-Myers’ arguments are nothing but a subterfuge to delay generic competition for Glucophage, specifically, and for other innovator products, generally.

required to do so before implementing new § 355a(o).

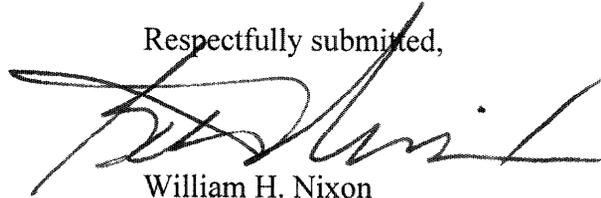
³ GPhA does not dispute that, in an appropriate case, FDA can seek outside input on drug approval decisions, such as by referring the matter to an appropriate expert advisory committee, 21 C.F.R. Part 14.

III. CONCLUSION.

For the reasons stated, Bristol-Myers' citizen petition is fatally flawed procedurally and is without merit substantively. It is nothing more than an effort to delay generic competition for Glucophage and other important generic products, in contravention of the clear intent of Congress. The relief Bristol-Myers seeks is counter to the public interest in having lower cost, safe and effective generic drug products available as soon as possible. For these reasons, GPhA and its members urge that FDA promptly deny Bristol-Myers' petition.

GPhA appreciates this opportunity to provide its views on behalf of the entire U.S. generic pharmaceutical industry.

Respectfully submitted,

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William H. Nixon
President and CEO

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* Call for Confirmation

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