

# REPLY

## Generic Pharmaceutical Association

### Submission to FDA

Symposium on the Hatch-Waxman Act  
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The central problem with the generic drug approval process is the abuse of the Orange Book patent listing provisions of the Hatch-Waxman Act to suppress generic competition. In its submission, PhRMA attempts to divert attention from this issue by accusing FDA of a bias toward the generic drug industry that has resulted in an erosion of drug approval standards, among other pernicious effects. The specifics of PhRMA's allegations are without substantive merit; instead they are a catalogue of PhRMA company complaints that FDA has justifiably rejected on scientific or legal grounds, with the backing of the courts when challenged.

PhRMA is satisfied with FDA's implementation of the patent listing standards of the FDCA. This is understandable, because FDA has ceded its authority in this area to PhRMA's members, the brand-name companies. The brand-name companies have used their *de facto* control of Orange Book patent listings as though they are entitled, as a matter of law, to block competition indefinitely despite the expiration of applicable patent rights and non-patent marketing exclusivities. This anti-competitive objective is inconsistent with the intent of Congress as embodied in the Hatch-Waxman Act. As discussed in GPhA's principal submission, the goal of that statute is to establish a generic drug program at FDA with sufficient resources and legal authority to facilitate the expeditious approval of lower-cost generic drugs after the expiration of generous periods of market exclusivity for the brand-name drug – exclusivity which the Hatch-Waxman Act extended by increasing patent terms and by providing for other, non-patent exclusivities. Congress specifically envisioned that when these applicable protections came to an end, the balance would shift in favor of public access to less costly generic drugs.

In enacting a generic drug program into federal law, Congress intended that consumers would benefit in two ways. First, consumers would benefit from brand-name company investments in research and development of innovative therapies that would be prompted by longer patent terms and non-patent exclusivity. Second, consumers would benefit from quicker access to lower-priced generic drugs that would become available immediately after the expiration of protected marketing periods for brand-name products.<sup>1</sup>

The first goal of Hatch-Waxman has been met. Brand-name drug companies continue to be among the most profitable enterprises in the country.<sup>2</sup> Drug prices outpace the Consumer Price Index by 300

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<sup>1</sup> In this reply, we will refer to GPhA's opening submission as "GPhA\_\_" and to PhRMA's opening submission as "PhRMA\_\_." We do not attempt in this reply to address all the misstatements in PhRMA's original submission that present a distorted description of the scope and purpose of the Hatch-Waxman Act.

<sup>2</sup> PhRMA disingenuously suggests that its current interpretation and application of the Hatch-Waxman Act should not change because it would decrease its members' incentive to spend money on research and development. However, this is precisely the same argument proffered by PhRMA in 1984 when the Hatch-Waxman Act was enacted. Indeed, PhRMA now boasts (PhRMA 4) that spending on research and development has increased *almost 1000 percent* since 1984. As is typically the case with the American economy, competition spurs growth rather than hinders it.

percent. Since 1988, the return on equity for the five biggest brand-name companies – Merck, Eli Lilly, Pfizer, Pharmacia, and Schering-Plough – has averaged 30 percent per year.<sup>3</sup> The patent extensions and other exclusivities granted by the Hatch-Waxman Act and subsequent laws have helped to ensure that brand-name companies are more than generously rewarded for their innovations.

The second goal of the Hatch-Waxman Act, expedited consumer access to affordable prescription drugs, is in serious jeopardy due to the efforts of PhRMA members to extend their market protections beyond where Congress intended them to stop. As GPhA discussed in its opening submission, these efforts include abuses of the Orange Book listing process, the Hatch-Waxman Act's 30-month stay and three-year exclusivity provisions, and the FDA citizen petition process.<sup>4</sup>

Contrary to PhRMA's contentions, the tactics of its members are not legitimate efforts to protect intellectual property rights. The Hatch-Waxman Act established (and extended) the scope of pharmaceutical market protections, and yet the brand-name companies are seeking to broaden these protections *beyond* what was contemplated by Congress, to the detriment of the other side of the statutory equation. In short, the brand-name companies endorse the intellectual property protections provided in Hatch-Waxman, but have sought to undermine the competition from generic drug products that the statute contemplated.

Unfortunately, to a significant degree, the brand-name companies have been successful in their efforts. According to a recent study from the National Institute of Health Care Manufacturers Foundation, average market exclusivities for brand-name products have increased in recent years by approximately 50 percent (from approximately 12 years to over 18 years). Similarly, the average patent term for these products has increased by almost 100 percent in the last two decades (from 8.1 years to 15.4 years). These increases are due in no small part to the aggressive efforts by brand-name companies to undermine the Hatch-Waxman regime.

PhRMA contends in its original submission that FDA has improperly "tilted" the Hatch-Waxman balance in favor of the generic companies. This contention is wholly unpersuasive and contrary to the available data. According to a 1998 Congressional Budget Office report, brand-name company sales

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At the same time, FDA should view with skepticism PhRMA's claims that it costs more than \$800 million in research and development to develop a new drug. PhRMA 17. According to a study by Public Citizen, the actual after-tax spending on each new drug (including failures) approximates \$110 million, about one-seventh of what PhRMA claims. Public Citizen Congress Watch, "Rx R&D Myths: The Case Against the Drug Industry's R&D 'Scare Card,'" July 2001, at i.

<sup>3</sup> John Carey and Amy Barrett, "Drug Prices: What's Fair?" *Business Week Online*, December 10, 2001 ("BW Online"), available at [http://www.businessweek.com/magazine/content/01\\_50/b3761001.htm](http://www.businessweek.com/magazine/content/01_50/b3761001.htm).

<sup>4</sup> According to one news article, even some drug company executives have characterized the brand-name efforts to broaden their monopolies as "brazen" and "embarrassing." *BW Online*, *supra*.

increased from \$17 billion to \$57 billion between 1983 and 1995; at the same time, generic substitution rates, which experts expected to reach up to 65 percent, continue to hover at around 40 percent.<sup>5</sup> The Hatch-Waxman balance has indeed been distorted. But it has been distorted in favor of brand-name companies that are permitted to act in a manner contrary to the statute's text and purpose. To the extent that FDA has upheld the generics' interpretation of the Hatch-Waxman Act, the Agency has remained faithful to Congress' goal of providing timely consumer access to affordable medicines after a *defined* period of brand-name exclusivity.

Some of the brand-name-company abuses of the Hatch-Waxman process can only be addressed through legislation, and GPhA supports the Schumer-McCain bill (S. 812) that would abolish the automatic 30-month stay and instead put brand-name companies on the same footing as other plaintiffs in patent infringement cases. But some of the abuses of the Hatch-Waxman system can be curtailed administratively. FDA should promptly consider and adopt the measures GPhA recommends. At stake are billions of dollars paid by the American consumer and third-party payers, including the federal government.

We address the specific contentions in PhRMA's brief below.

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<sup>5</sup> One study, by Tim R. Covington, Executive Director of The Managed Care Institute at Samford University, has determined that a mere 1 percent increase in the nation's generic utilization rate would generate payer savings of \$1.3 *billion* each year.

## **II PhRMA's Claim of Eroded Standards for ANDA Approvals Is False.**

PhRMA paints a distorted picture of Hatch-Waxman's "sameness" requirement and of FDA's application of that requirement in the ANDA approval process, arguing that FDA has not required that generics be the "same" as their brand counterparts, and that there has been an "erosion" of generic approval standards. This is patently erroneous. Generic approval standards have not eroded. They have evolved and become more demanding based on sound scientific and pharmaceutical principles, and advances in the field. FDA's implementation of these heightened approval standards has ensured that consumers will receive therapeutically equivalent generic products that are the "same" as the brand counterparts in safety, efficacy, and quality.

PhRMA criticizes several FDA approval decisions for supposedly violating principles of "sameness."<sup>6</sup> Its complaints incorrectly assume that "same" and FDA's term "identical" (21 C.F.R. § 314.92(a)(1)) must be applied literally to preclude any and all differences, no matter how medically inconsequential. This would lead to absurd results. FDA must have the discretion to give these terms a reasonable interpretation. Such flexibility is essential for applying the sameness requirement in a sensible way to diverse factual situations and for meeting the challenges posed by new technologies and scientific learning.

PhRMA also contends that there has been a similar "erosion" of the "same" labeling requirement. Yet, given the fact that the FDCA, and its implementing regulations, specifically allow generic drug labeling to differ from the listed drug labeling in certain respects, it is unclear how these permissible differences constitute an erosion in FDA's standards for approval. As GPhA demonstrated in its original submission, and as illustrated in more detail in Section VI of this reply, FDA merely enforces the applicable statutory standard as drafted and contemplated by Congress. For example, FDA has interpreted differences in labeling caused by the omission of labeling statements protected by exclusivity to be labeling "differences" that are permitted under the statute.<sup>7</sup> Two different Circuit Courts of Appeals have upheld this Agency position,<sup>8</sup> which is entirely consistent with the omission of indications protected by patents under Section 505(j)(2)(A)(viii) and underlying congressional intent.

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<sup>6</sup> *E.g., Sero Laboratories Inc. v. Shalala*, 158 F.3d 1313 (D.C. Cir. 1998) (upholding FDA determination).

<sup>7</sup> *See* 21 C.F.R. §§ 314.94(a)(8)(iv), 314.127(a)(7).

<sup>8</sup> *Bristol-Myers Squibb Co. v. Shalala*, 91 F.3d 1493 (D.C. Cir. 1996); *Zeneca, Inc. v. Shalala*, 1999 U.S. Dist. LEXIS 12327 (D. Md. Aug. 11, 1999), *aff'd*, 213 F.3d 161 (4th Cir. 2000).

On the subject of “same” dosage forms, the examples cited by PhRMA in its submission involve FDA’s use of appropriate judgment in a few isolated situations. FDA’s policy on dosage-form classification has been remarkably consistent and has been upheld by the courts.<sup>9</sup> The Agency has provided a degree of consistency in its approach by placing all drug products within one of the dosage forms enumerated in the Orange Book, unless there was a scientifically valid reason for not doing so. This clear policy has proven to be relatively easy to implement, yet sufficiently flexible to address scientifically valid product differences.

Concerning the issue of bioequivalence, PhRMA is relitigating an issue that was settled years ago. All courts that have examined this issue have upheld FDA’s regulations defining “bioequivalence” and the Agency’s statutory authority to use appropriate scientific methods (including *in vitro* and confirmatory studies) for determining bioequivalence beyond the simple “rate and extent of absorption” blood level methodology.<sup>10</sup> PhRMA’s assertion that FDA created its bioequivalence policy out of whole cloth following enactment of the Hatch-Waxman Act (PhRMA 27-29) ignores Congress’ clear intent to codify FDA’s pre-1984 bioequivalence criteria, which were set forth in Agency regulations issued in 1977.<sup>11</sup> In reviving this bioequivalence issue as an example of FDA’s “pro-generic tilt” and eroding drug approval standards, PhRMA is rehashing FDA’s judicially-validated scientific judgment that bioequivalence can be reliably assured by means other than measuring blood levels.

PhRMA’s criticisms of FDA’s generic drug approval process are not only demonstrably false, they also seriously undercut the public’s confidence in the Agency, as well as in generic drugs. PhRMA’s suggestion that generic drugs and manufacturing facilities do not meet the same standards as brand drugs is flatly wrong. And its assertion that generic drugs manufactured with ingredients from overseas suppliers are inferior to brand drugs is grossly misleading: many brand manufacturers purchase ingredients from foreign sources, and whether they sell to GPhA or PhRMA members, foreign drug suppliers are subject to full FDA inspection for Good Manufacturing Practices and are held to the same standards as domestic manufacturers.

PhRMA’s anti-generic statements reflect a broader campaign by brand-name drug companies to disparage the generic drug industry. GPhA urges FDA to counteract these false messages by

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<sup>9</sup> See *Pfizer, Inc. v. Shalala*, 1 F. Supp. 2d 38 (D.D.C. 1998), *rev’d on other grounds* 182 F.3d 975 (D.C. Cir. 1999).

<sup>10</sup> See *Schering Corp. v. Sullivan*, 782 F. Supp. 645 (D.D.C. 1992), *vacated as moot, sub. nom., Schering Corp. v. Shalala*, 995 F.2d 1103 (D.C. Cir. 1993); *Schering Corp. v. FDA*, 866 F. Supp. 821 (D.N.J. 1994), *aff’d*, 51 F.3d 390 (3d Cir. 1995), *cert. denied* 116 S. Ct. 274 (1995); *Glaxo, Inc. v. Shalala*, No. 94-1323(JHG) (D.D.C. July 22, 1994).

<sup>11</sup> See H.R. Rep. No. 98-857, 98th Cong., 2nd Sess. Pt. 1, at 31; *see also* 21 C.F.R. 320.1(e) (1977).

undertaking comprehensive, national public education programs on a yearly basis to accomplish two goals: (1) to correct misinformation disseminated by the brand industry, its members and/or agents; and (2) to educate consumers on the Agency's generic approval process and the socioeconomic benefits of affordable pharmaceuticals. As discussed in its opening submission (GPhA 33), GPhA also urges the Agency to initiate meaningful enforcement action, such as requiring corrective advertising or "dear healthcare professional letters," when brand firms engage in anti-generic promotional tactics and national or state campaigns. These actions, if implemented, will increase the likelihood that consumers can fully realize the economic and therapeutic benefits of affordable pharmaceuticals.



### **III GPhA Supports FDA's Efforts to Curb the Improper Use of Citizen Petitions.**

GPhA's principal brief describes the use by brand-name companies of FDA citizen petitions to delay the Agency's approval of ANDAs. GPhA 32. FDA has itself proposed to limit the use of citizen petitions aimed at administrative actions pending for decision.<sup>12</sup> GPhA urges the Agency to finalize its proposed regulations as soon as possible.

PhRMA suggests in its submission that limitations on the use of citizen petitions will prevent FDA from receiving important scientific and medical information. PhRMA 32. This is incorrect. GPhA does not contend that the Agency should ignore such information, nor does FDA's proposal foreclose outside comment on a pending ANDA. Indeed, FDA will continue to receive information relevant to a pending ANDA as part of its review of that ANDA, from brand-name companies and any other sources.

What FDA's proposed regulations *will* change is the use of the formal petition process to unduly delay ANDA approvals and to thwart the goals of the Hatch-Waxman Act. Some citizen petitions are plainly filed with that purpose in mind, and Agency review of a citizen petition challenging prospective ANDA approval can be time-consuming. Often a written response is required which is prepared by divisions of the Agency not subject to the deadlines applicable to generic drug reviews. Citizen petitions are also improperly used as an implicit threat to FDA that a brand-name company intends to sue the Agency to challenge an ANDA approval. FDA's proposed limits on citizen petitions would address this improper use of the petition process.

GPhA urges FDA to be mindful of the use of litigation threats to stall ANDA approvals, whether those threats are made by the filing of a citizen petition or otherwise. We understand that where a drug company has made a last minute threat of litigation, there is a temptation to delay the approval to allow Agency attorneys time to prepare for the lawsuit. We urge the Agency to recognize the inappropriateness of such delays and to either anticipate the need for preparation so that it may be completed concurrently with timely ANDA approval or, in extraordinary circumstances, to complete such preparation and to issue the approval on a priority basis.

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<sup>12</sup> 64 Fed. Reg. 66822 (Nov. 30, 1999).

## REPLY

In arguing that FDA should not disturb such abuses of the petition process, PhRMA attempts to cloak itself in the mantle of the public interest, arguing that “principles of open government” give PhRMA members the right to file citizen petitions. However, FDA’s proposal recognizes that brand-name companies may at any time submit information to the Agency on an ANDA, thereby preserving PhRMA members’ legitimate open government rights, while at the same time limiting the opportunities to delay ANDA approvals.

**IV Under Section 505(b)(2), NDAs May Be Based on any Publicly Available Data that Supports a Finding of Safety and Effectiveness for a Brand-Name Drug.**

PhRMA argues that FDA is precluded from approving 505(b)(2) NDAs based on FDA's previous finding of safety and effectiveness for a brand drug. PhRMA 34. PhRMA asserts that there is no textual support for FDA's position within the FDCA and that Congress, in enacting the Hatch-Waxman Act, merely intended to codify FDA's pre-1984 paper NDA policy for duplicates of post-1962 drug products. PhRMA 33.<sup>13</sup>

PhRMA's argument, however, ignores a fundamental tenet of statutory construction: provisions of the same enactment must be interpreted so as not to render one provision superfluous. *See Pennsylvania Dep't of Public Welfare v. Davenport*, 495 U.S. 552, 562 (1990). PhRMA's interpretation violates this principle because it would render section 505(b)(2) redundant and unnecessary. Congress provided an approval mechanism for duplicates of post-1962 approved drugs under section 505(j). Therefore, section 505(b)(2) must have been intended to apply to drugs that are not duplicates of approved drugs. This intent is clearly apparent from the structure of section 505. By placing the provision at issue within the construct of section 505(b), rather than within 505(j), Congress clearly intended that 505(b)(2) applications (like pre-1984 paper NDAs) would be subsets of "full" NDAs as described in section 505(b)(1), as opposed to subsets of section 505(j) applications. Thus, Congress plainly intended to provide FDA with the authority to determine when an application met the "full reports of clinical investigations" requirement of section 505(b)(1).

Furthermore, the FDCA specifically allows any applicant submitting a 505(b)(2) or 505(j) application to obtain "safety and effectiveness data and information" from a 505(b) application once an ANDA is, *or could be*, approved for the drug that is referenced in the NDA. 21 U.S.C. § 355(l)(5). Thus, on or after that date, there is no logical basis for FDA *not* to permit reliance in a 505(b)(2) application on FDA's "finding" that is fully described in those publicly available documents. A careful reading of section 505(b), together with sections 505(c)(3)(D), 505(j) and 505(l), clearly establishes that section 505(b)(2) is not merely a codification of the Agency's paper NDA policy, but is an approval mechanism for any drug product – regardless of the drug product's characteristics – that relies on investigations

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<sup>13</sup> The "paper NDA" policy is described in an FDA internal memorandum written by Dr. Marion Finkle (published at 46 Fed. Reg. 27396 (May 19, 1981)). The policy applied only to duplicate drug products of post-1962 drugs. The term "duplicate drug product" in the "paper NDA" context consisted of "drug products which contained an active ingredient identical to an already marketed drug product first approved for marketing after 1962 in the same or closely related dosage form, and offered for the same indications as those of the already marketed drug product." 54 Fed. Reg. 28872, 28890 (July 10, 1989). The policy addressed the Agency's perceived inability to approve ANDAs for duplicates of drug products approved after 1962. *See* 46 Fed. Reg. at 27396. FDA believed it could lawfully approve ANDAs based on the data relevant to NDAs approved prior to the enactment of the Drug Amendments of 1962, but there was considerable debate over FDA's authority to rely on data in post-1962 NDAs. Therefore, FDA adopted the "paper NDA" policy to permit approval of duplicates of post-1962 drugs based on published scientific literature. FDA's failure to adopt an ANDA policy for post-1962 drugs was a principal reason leading to the enactment of the Hatch-Waxman Act. *See* H. R. Rep. 98-857, Pt. 1 at 16.

which the applicant has not conducted or sponsored, or as to which it has not obtained a right of reference. 21 U.S.C. § 355(b)(2).

PhRMA's citation of FDA's position on this issue is targeted at the Agency's 1999 guidance document, PhRMA 33, but PhRMA fails to note that the Agency's position was first proposed in 1989, ten years earlier. At that time, FDA considered the very same arguments PhRMA is now making when promulgating the regulations implementing section 505(b)(2). FDA concluded that section 505(b)(2) was *not* limited by the Agency's previous "paper NDA" policy. *See* 21 C.F.R. § 314.54. Specifically, as early as 1989, FDA stated that:

[d]espite certain similarities between section 505(b)(2) of the act and the 'paper NDA policy,' [section 505(b)(2)] *is broader than* the paper NDA policy. Although the legislative history of the [Hatch-Waxman Act] refers to 'paper NDAs' in discussing the applications described in section 505(b)(2) and 505(c)(3)(D) of the act, the language of these provisions does not limit the applications described to duplicates of already approved products.

54 Fed. Reg. at 28890 (emphasis added). In other words, when interpreting the Hatch-Waxman Act, FDA has permitted section 505(b)(2) NDA sponsors to reference both published scientific literature and prior Agency findings of a drug's safety and effectiveness. 57 Fed. Reg. 17950, 17952 (Apr. 28, 1992). The Agency's conclusion thirteen years ago was based on the same sound principles of statutory interpretation that are applicable today. Accordingly, it is inconceivable, as PhRMA contends, that Congress intended section 505(b)(2) to be limited in scope to duplicates of already approved drug products.

**V PhRMA’s Laissez-Faire Defense of FDA Patent Listing Rules and the 30-Month Stay Is Unavailing.**

**A Contrary to PhRMA’s Contention, the Current Orange Book Listing Process Should be Significantly Reformed.**

PhRMA agrees with GPhA that the listing of patents in the Orange Book is critical, because patent listing triggers the certification, notification, and 30-month stay provisions of the Hatch-Waxman Act. PhRMA 35. While PhRMA does not mention that there has been abuse of the Orange Book listing process, it notably does not deny that abuses have occurred. Instead, PhRMA contends that the listing criteria are ambiguous (PhRMA 35), that the “controversy surrounding the listing of . . . patents [that do not apply to the approved product] does not indicate that the listings are necessarily improper” (PhRMA 36), and that “[p]ublic attention has focused on a relatively small number of disputed patent infringement cases arising at the margin.” PhRMA 1. In other words, according to PhRMA, if there is a “problem” with inappropriate Orange Book patent listings, it is small, and the courts are addressing it.

Nothing could be farther from the truth. There is a major problem of Orange Book abuse, and the courts and FDA are *not* addressing it. The problem is a major one for two reasons. First, brand-name companies focus *their* attention on defending major products, *i.e.*, the widely prescribed blockbuster drugs that account for a disproportionately large part of annual pharmaceutical sales. Thus, the resulting legal controversies are not merely isolated cases “at the margin,” but instead involve drug products that affect consumers the most and for which, therefore, Congress believed timely generic competition was also most important.

The second reason there is a major problem of Orange Book abuse is that, free from scrutiny from either FDA or the courts, brand-name companies have interpreted the statutory patent listing criteria very loosely. The result is that PhRMA’s members list irrelevant patents in defense of brand-name franchise products through the use of conclusory phrases like “covers the formulation.” So long as FDA refuses to look at what is being submitted, brand-name companies can continue to list just about any patent in the general vicinity of an NDA drug.

PhRMA's suggestion that the courts "are addressing" this problem flies in the face of two fundamental realities: first, FDA declines to exercise any responsibility for applying the statutory patent listing standard; and second, the courts refuse to acknowledge any effective right of action by an ANDA applicant to require the delisting of an improperly listed patent.<sup>14</sup>

As a solution to this problem of Orange Book abuse, GPhA proposes that FDA strengthen the NDA holder's patent listing declaration, and that FDA, based on that declaration, fulfill its obligation to refuse an Orange Book listing of any patents determined to be ineligible for listing in accordance with the applicable FDCA standard. *See* GPhA 19-25.

PhRMA defends FDA's current laissez-faire system. If there is controversy, it says, it results from the "ambiguity" of the patent submission criteria in the FDCA. According to PhRMA, the "primary ambiguity" is the requirement that the patent holder list patents that claim the "drug." PhRMA 35-36. PhRMA is correct that "drug" can mean different things depending on where it appears in the FDCA, but there is *no* ambiguity in the requirement that, to be listed, a patent must claim the drug "for which the applicant submitted *the application*," *i.e.*, the NDA. 21 U.S.C. § 355(b)(1) (emphasis added). Whether the patent is on the drug formulation, or on the active ingredient in the drug, is not, as PhRMA invites the reader to believe, the issue underlying current Orange Book abuses. Instead, the issue is whether the listed patent claims anything at all that is "the subject of" the NDA that FDA has actually approved. *See* 21 C.F.R. § 314.53(b).

It is this issue that the FTC has asked FDA to address, an invitation that, to date, FDA has declined. GPhA 23. GPhA believes that FDA both can, and must, apply the listing criteria of 21 U.S.C. §§ 355(b)(1) and 355(c)(2). This does not involve resolving an ambiguous statutory term but instead requires FDA to determine what relationship must exist between a patent and an NDA-drug in order for the patent to qualify for an Orange Book listing. This is exactly the type of situation in which agencies are expected to exercise their administrative expertise, *i.e.*, where it is necessary to particularize the general requirements of a statute to facilitate compliance and thereby carry out the intent of Congress.

Such regulations are well within both FDA's authority and its experience in administering the Hatch-Waxman Act. FDA has the necessary expertise to decide what is "the subject of" an NDA, and the expanded declaration GPhA recommends will, if adopted by FDA, provide sufficiently detailed information about submitted patents to allow the Agency to determine if a patent is eligible for listing. FDA has an obligation to do this: as one court has stated, "[i]t is the FDA's job to determine whether to

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<sup>14</sup> A generic drug applicant can sue FDA. *See Biovail Laboratories, Inc. v. Andrx Pharm., Inc.*, No. 01-1650, 02-1025 (Fed. Cir. January 17, 2002). But courts have deferred to FDA's administrative neutrality under prevailing judicial review precedents, such as *Chevron U.S.A., Inc. v. Natural Resources Defense Council*, 467 U.S. 837 (1984). *See Watson Pharm., Inc. v. Henney*, 2001 U.S. Dist. LEXIS 2477, at \*4 (D. Md. January 18, 2001).

list or delist a patent.”<sup>15</sup> The Orange Book listing standard is in the FDCA, not in the patent statute, Title 35, U.S. Code. FDA cannot fulfill its obligation to administer the FDCA by continuing to treat the listing standard as outside the Agency’s jurisdiction because it relates to patents. The standard may *relate* to patents, but it is *in* the FDCA. It has FDCA consequences. And it consists in part of a regulatory authorization – “the application,” *i.e.*, the NDA – that is exclusively within FDA’s area of expertise.

PhRMA is wrong in asserting that FDA has no role in the patent listing process (PhRMA 38-39). The statutory language imposing the patent submission requirement is in the same section of the drug approval provision as the requirement for safety and effectiveness information, *i.e.*, 21 U.S.C. § 355(b)(1). There is nothing in that section to support the conclusion that FDA is authorized to evaluate safety and effectiveness data but is prohibited from evaluating patent information to determine if it meets the standard *of the FDCA* for listing in the Orange Book. Logically, it is the opposite conclusion that the structure of the FDCA requires: if FDA reviews one category of information submitted under § 355(b)(1), it can and should review another that is submitted under the same provision.

Of course, the review must relate to the statutory standards FDA is authorized to apply. In the case of safety and effectiveness data, the standard is in 21 U.S.C. § 355(d). In the case of patent information, the standard is stated in § 355(b)(1) itself, *i.e.*, the patent must be one that “claims the drug for which the applicant submitted the application,” or that “claims a method of using such drug.” Applying this standard does not involve “matters of substantive patent law,” as to which FDA “has no statutory franchise.” *Watson Pharm., Inc. v. Henney, supra*, at \*7.<sup>16</sup> It involves comparing the claims of the patent to the “drug that is the subject of the new drug application,” 21 C.F.R. § 314.53(b), and, therefore, pertains to “matters of FDCA law.” FDA has both a statutory franchise to resolve such matters, and a corresponding duty to do so.

PhRMA’s argument (PhRMA 39) that FDA cannot evaluate a proposed Orange Book patent listing because the FDCA requires FDA to publish (“shall publish”) the patent information is a *non sequitur*. The fact that FDA must publish information has nothing to do with whether FDA is authorized to review the information. FDA is required to publish and maintain a list of approved drugs, 21 U.S.C. §§ 355(j)(7)(A)(i) and 355(j)(7)(A)(ii), but, obviously, FDA reviews the NDAs before publishing them in the list of “approved drug products,” *i.e.*, the Orange Book. FDA should likewise review patent

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<sup>15</sup> *Andrx Pharm., Inc. v. Biovail Corp.*, No. 01-6194-CIV-DIMITROULEAS (S.D. Fla. March 6, 2001), Omnibus Order, at 9, *rev’d on other grounds*, No. 01-1650, 02-1025 (Fed. Cir. January 17, 2002).

<sup>16</sup> PhRMA’s reliance on the *Watson* decision (PhRMA 39) is misplaced. There, the court agreed with FDA that the Agency has a “limited, ministerial role in patent fights,” but the court did not say that the “limited” role FDA does, in fact, have precludes the Agency from reviewing proposed Orange Book patent listings to determine that the FDCA’s listing standard is met. GPhA recommends that FDA expand its role to include that very narrow exercise of judgment.



declaration submissions to determine whether patents are eligible for Orange Book listing. FDA will be able to do so if it implements GPhA's recommendations, including a broadened patent declaration.

The current anarchic situation, by contrast, is unacceptable from several points of view. First, it is unfair to generic drug companies and to American consumers. Regardless of whether the automatic 30-month stay provision of Hatch-Waxman is justified on its own terms, there is no justification whatsoever for allowing it to be invoked unilaterally by the NDA holder/patent owner with *no* mediation by FDA in the form of applying the FDCA patent listing standard in accordance with its own terms. PhRMA extensively (and baselessly) criticizes FDA for failing to apply the bioequivalence standard of Hatch-Waxman in the way PhRMA believes is required (PhRMA 27-29), but PhRMA cannot complain that FDA is failing to impose bioequivalence requirements at all. When it comes to FDA's refusal to apply the patent listing standard, however, PhRMA endorses FDA's complete neutrality.

Second, the predictable result of FDA's failure to take responsibility for the patent listing standard is that ineligible patents are, in fact, listed. Even PhRMA has difficulty saying this is not so: the strongest language PhRMA can muster is that "the listing of such patents does not indicate that the listings are necessarily improper." PhRMA 37. GPhA will take this as a concession by PhRMA that the listings are not necessarily proper, either. Listing irrelevant patents is unfair to the public. Orderly litigation of brand-name companies' patent rights may be, as PhRMA says (PhRMA 14), a "purpose" of the Hatch-Waxman Act's 30-month automatic stay provision, but only rights related to patents that qualify for Orange Book listing are proper objects of that purpose. Conversely, if ineligible patents are listed, another important goal of the Hatch-Waxman Act is defeated: the goal of "get[ting] generic drugs into the hands of patients at reasonable prices – fast." *In re Barr Labs., Inc.*, 930 F.2d 72, 76 (D.C. Cir. 1991), *cert. denied*, 502 U.S. 906 (1991).

Finally, FDA's unwillingness to engage in even minimal review of patent listings produces widespread uncertainty about what is permissible, an uncertainty that puts the brand-name companies themselves in a dilemma. PhRMA cites two district court decisions relating to Orange Book listings. PhRMA 37. Neither case provides meaningful guidance to the regulated industry as to what the "claims the drug" standard means.<sup>17</sup> FDA did not participate in either case, and, of course, it has no regulatory standards other than that the patent must claim the drug that "is the subject of" the NDA. Until FDA provides

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<sup>17</sup> *Zenith Labs., Inc. v. Abbott*, No. 96-1661 (D. N.J. Oct. 2, 1997), is an unpublished decision. Further, the *Zenith* court erroneously stated that FDA had "approved" the listing of the subject patents in the Orange Book (footnote 6, *supra.*). As FDA is aware, the Agency does not currently "approve" the listing of patents. *Ben Venue Labs., Inc., v. Novartis Pharm. Corp.*, 10 F. Supp. 2d 446 (D. N.J. 1998), is also of no assistance in this analysis. The facts of that case are entirely different and involve the propriety of listing a patent on an intermediate active ingredient drug substance of the NDA holder's approved drug product.



more specific guidance, brand-name companies that want to exercise restraint about Orange Book listings will have no coherent rationale from FDA or the court system for doing so.

The need for FDA to give effect to the Orange Book patent listing standard is pointed up by PhRMA's perfunctory justification for the Agency's uncritical acceptance of any patent labeled as a "product-by-process" patent. PhRMA 38. As GPhA has explained (GPhA 23-25), not all "product-by-process" patents are the same. Some do, in fact, claim a drug product. Others, however, are just process patents in disguise as product patents, and these process patents clearly do not qualify for Orange Book listing. See 21 C.F.R. § 314.53(b). In the pharmaceutical area, we are not aware of "product-by-process" patents that are anything other than process patents in disguise. This is because such patents do not claim a new drug product or a new drug substance. Rather, these pharmaceutical product-by-process patents claim a novel process-based limitation. PhRMA's position is that, if the NDA holder calls the patent a "product-by-process" patent, then "FDA has no authority to refuse" to list it. This is not so. FDA must refuse to list any process patent which the NDA holder attempts to submit for listing. PhRMA's position – reflecting current FDA policy – that FDA must *ipso facto* accept the NDA holder's representation that a process patent meets the listing standard demonstrates, by its very implausibility, why FDA cannot continue to be passive about whether patent submissions qualify for Orange Book listing.

In sum, due to FDA's neutrality, the current Orange Book patent listing system has become more a tool for product life cycle management for high revenue blockbuster drugs than a means of giving notice to generic drug companies or a vehicle for the "orderly" resolution of patent disputes.<sup>18</sup> FDA cannot completely eliminate Orange Book abuse. But, by accepting GPhA's recommendations, the Agency can at least impose some limits on the extent to which some brand name companies are able to manipulate Orange Book patent listings.

#### **B      Congress' Intent Was Clearly to Permit Only One 30-Month Stay per ANDA.**

In its submission (GPhA 14-19), GPhA contended that the language, legislative history and purposes of the Hatch-Waxman Act all clearly established that Congress intended only one 30-month stay to apply for each ANDA. PhRMA claims that the text of Hatch-Waxman proves just the opposite – that the

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<sup>18</sup> The idea that "FDA has adopted a pro-generic interpretation of the listing requirements" for formulation patents (PhRMA 36) is unsupported by the example cited, *Pfizer, Inc. v. FDA*, 753 F. Supp. 171 (D. Md. 1990). The patent at issue in that case claimed a drug formulation that was not the subject of Pfizer's NDA. The patent thus did not claim "the drug for which the applicant submitted the application." FDA simply applied the words in the statute – as PhRMA says the Agency must – to conclude that the patent was not eligible for listing.

statute contemplates more than one 30-month stay per ANDA. A close review of the statutory language demonstrates that GPhA is correct.

Both PhRMA and GPhA rely on 21 U.S.C. § 355(j)(5)(B)(iii). The purpose of this statutory provision is to establish when an ANDA approval becomes effective. As GPhA has noted, section 355(j)(5)(B)(iii) states unequivocally that an ANDA approval *shall* become effective after the expiration of *the* 30-month stay triggered by the *original* Paragraph IV certification (“the notice provided under paragraph (2)(B)(i)”). Once this mandatory approval has taken place, FDA regulations demonstrate that there is simply no opportunity for an additional 30-month stay. *See* 21 C.F.R. §§ 314.95, 314.107(b)(3).

PhRMA suggests in its brief that the statute mandates a 30-month stay whenever a Paragraph IV certification is filed. It neglects to note, however, that this mandate only applies to stays triggered by the *original* certification. There is no question that *this* stay is mandatory, but to extend this reasoning to cover additional stays is inconsistent with the language of the statute.

PhRMA’s argument that the Hatch-Waxman Act permits multiple stays per ANDA also ignores the legislative history and purposes of the statute. As GPhA demonstrated in its original submission, Congress did not intend pending patent litigation to delay the public’s access to lower-priced generic drugs for more than 30 months, and in fact debated whether to make the stay 18 months or 30 months – a debate that would have been unnecessary had more than one stay been permitted. In short, the Hatch-Waxman Act’s legislative history and purpose make clear that there can only be one 30-month stay per ANDA.

**VI Contrary to PhRMA, FDA Should Reaffirm, Not Revisit, Its Position Regarding Three-Year Exclusivities.**

Contrary to PhRMA's assertions (PhRMA 45), FDA's policy does not "undermine the utility" of the statutory provision providing for three-years of exclusivity for certain NDA supplement changes, nor does this provision deny exclusivity to NDA supplements that meet the statutory criteria. Rather, FDA reasonably interprets the statutory criteria in a way that gives effect to the intent of Congress to provide precisely targeted exclusivity to those applicants who make innovations in already approved drug products. This exclusivity provides an incentive for drug development, even if it is a more modest incentive than PhRMA would prefer. In addition, FDA grants this exclusivity more broadly than Congress intended, *i.e.*, to product changes that do not represent "important innovations." This unjustified administrative expansion of three-year exclusivity is of concern to GPhA, as explained in our original submission. GPhA 28-29. By contrast, PhRMA's concerns are with the restriction that Congress itself placed on three-year exclusivity.

PhRMA specifically takes issue with FDA's policy of allowing generic companies to omit protected labeling statements from their labeling, a policy that has been upheld by two Circuit Courts of Appeals.<sup>19</sup> In so doing, PhRMA attempts to cloud the issue by raising practice of medicine and state drug substitution issues.<sup>20</sup> Yet, the Hatch-Waxman Act specifically allow for generic products to omit indications of use from their labeling that are covered by method of use patents, and to bear different labeling from that of the brand drug due to the fact that the products are manufactured by different companies.<sup>21</sup> Moreover, both FDA and the courts have agreed that the statute allows generic applicants to omit labeling statements that are protected by patents or exclusivity.<sup>22</sup> Indeed, the U.S. Court of Appeals for the District of Columbia Circuit in *Bristol-Myers Squibb v. Shalala* addressed the very issue that PhRMA seeks to resurrect here:

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<sup>19</sup> See *Bristol-Myers Squibb Co. v. Shalala*, 91 F.3d 1493 (D.C. Cir. 1996); *Zeneca, Inc. v. Shalala*, 1999 U.S. Dist. LEXIS 12327 (D. Md. Aug. 11, 1999), *aff'd*, 213 F.3d 161 (4th Cir. 2000).

<sup>20</sup> As FDA has long recognized, the FDCA does not provide FDA with the authority to regulate possible substitution of a generic drug for the pioneer by doctors or pharmacists. See *Bristol Myers Squibb Co.*, 91 F.3d at 1496 (citing *Federal Trade Comm'n v. Simeon Mgmt. Corp.*, 391 F. Supp. 697, 706 (N.D. Cal. 1975)).

<sup>21</sup> See 21 U.S.C. §§ 355(j)(2)(viii), (j)(2)(A)(v).

<sup>22</sup> See 21 C.F.R. §§ 314.94(a)(8)(iv), 314.127(a)(7); *Bristol-Myers Squibb Co.*, 91 F.3d at 1500; *Zeneca, Inc.*, 1999 U.S. Dist. LEXIS 12327 at \*38.

Under [the brand-name company's] interpretation, every time a supplemental indication is added to the labeling of a pioneer drug, the manufacturer of the pioneer would get three more years of protection against the approval of any ANDA based upon that pioneer drug, including one that lists only the original indications(s) of the pioneer. By the way of contrast, under the Secretary's interpretation of the Act, a pioneer drug manufacturer that obtains approval for a supplemental indication based upon proprietary research will enjoy three years during which the FDA will not approve any ANDA that includes the supplemental indication.

91 F.3d at 1500. The D.C. Circuit proceeded to reject the brand-named company's interpretation as unduly broad. The Court of Appeals also rejected the argument that three-year exclusivity is worthless if an ANDA applicant can omit the protected labeling indication knowing that the product may still be substituted for the reference listed drug regardless of labeling. On that point, the court stated:

[The brand-name company] claims that economic reality renders the protection offered by the Secretary largely an illusion. Perhaps so, but why? By [the brand-name company's] own account, it is because the value of the protection the Congress most clearly conferred upon pioneers would be greater but for some state laws and health insurers that mandate substitution of generic drugs. *That is not a sufficient basis upon which to conclude that the Congress intended to confer upon the manufacturers of pioneer drugs the much broader protection that [the brand-name company] now seeks. Id.* (emphasis added).

Obviously, PhRMA does not like the outcome of the case law on this matter nor the actual "value" of the three-year exclusivity provision.<sup>23</sup> Yet these issues are well settled. Instead, the critical issue is whether a generic product that omits any aspect of a brand's labeling is safe and effective for its labeled indications.<sup>24</sup> If so, that product may be marketed notwithstanding a brand-name company's entitlement to three years of labeling exclusivity. PhRMA's objections with respect to the Agency's implementation of the three-year exclusivity provision are therefore without merit.<sup>25</sup>

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<sup>23</sup> Likewise, PhRMA's concerns over the Agency's draft guidance document on the reference of discontinued labeling are without merit (PhRMA 45-46). The draft guidance naturally flows from the Agency's current policy and from court decisions permitting labeling carve-outs and the referencing of listed drugs that were discontinued for reasons other than safety and effectiveness. *See* 21 C.F.R. § 314.161.

<sup>24</sup> We also note that PhRMA's allegation of "generic boosterism" concerning suitability petitions is misguided (PhRMA 46). FDA has very little discretion when reviewing suitability petitions. *See* 21 U.S.C. § 355(j)(2)(C). Thus, there is no merit to PhRMA's allegation that FDA is favoring the generic industry. Rather, FDA is merely implementing the plain language of the unambiguous suitability petition process contained in the FDCA, which sets forth a statutory mandate to approve suitability petitions unless they raise safety or efficacy concerns.

<sup>25</sup> Although FDA recognized in 1989 the underlying congressional intent of the three-year provision, FDA has broadly interpreted the provision in favor of the brand-name industry. Accordingly, the Agency has ignored the fact that the three-year provision includes special criteria intended to limit eligibility to significant innovations. 54 Fed. Reg. 28872, 28896 (July 10, 1989) (citing Cong. Rec. H9114, 9124 (daily edition Sept. 6, 1984) (statement of Rep. Waxman); Cong. Rec. S10505 (daily edition Aug. 10, 1984) (statement of Sen. Hatch)).

**VII Conclusion**

For the above reasons, as well as the reasons discussed in GPhA's initial submission, FDA should adopt GPhA's recommendations and reject the recommendations urged by PhRMA.



Generic Pharmaceutical Association (GPhA)