Generic Pharmaceutical Association (GPhA) Materials for January 30, 2002 Meeting with FDA

"I don't object to companies legitimately defending their patents. What I object to is the gaming of the system for the benefit of their bottom line at the expense of taxpayers, consumers, and seniors. They've had their patent protection, they've made their money."

-Vermont Governor Howard Dean
Boston Globe Online, December 26, 2001

"Today I call upon the brand-name industry to cease and desist from inventing new games, that they work with us to re-balance the brand-name and generic system, that they return to the scientific research that they are good at and that has been their real contribution."

-Representative Henry A. Waxman
November 20, 2001

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January 18, 2002

Mr. Daniel Troy
Chief Counsel
Food and Drug Administration
Room 6-57 (GCF-1)
5600 Fishers Lane
Rockville, Maryland 20857-1706

Dear Mr. Troy:

The Generic Pharmaceutical Association (GPhA) submits the attached document which responds to your request for materials that will be used in a meeting scheduled for January 30, 2002 with various industry representatives. GPhA's members are looking forward to making progress on resolving serious problems with the regulatory and statutory framework which governs the review and approval of the abbreviated new drug applications by the Food and Drug Administration (FDA). We believe that framework has become seriously flawed in its application of both legislative intent and the plain meaning of the statutory
language. As a result, consumers are denied timely access to safe and effective
generic medicines.

We wish to emphasize that it is our view the FDA cannot unilaterally resolve all
of the problems which presently impede consumer access to generic medicines.
Changes in technology and research methodologies, and a variety of legal
strategies used by regulated companies since the enactment of the Hatch-Waxman
Act have required FDA and the Courts to make piecemeal adjustments to the Act.
Cumulatively, these changes have produced a nearly impossibly complex and
contradictory review process that is unpredictable and subject to manipulation and
abuse. The system begs for a more thorough reform than is possible through
simply revising existing regulations and policies.

GPhA welcomes the dialogue you have invited our industry to participate in, and
we strongly believe that some interim regulatory changes are needed and should
be implemented. However, there is a real danger that the process of engaging in
this dialogue could be used by some industry representatives as a justification to
delay legislative reforms which otherwise would be considered and implemented
by the U.S Congress. FDA should exercise care that GPhA's discussions with you
not have the appearance of, or become an actual impediment to, legislative
reforms that are needed to address critical elements of the generic drug approval
process. In particular, we are concerned that the discussions may be used by the
brand industry who benefit from the present dysfunctional regulatory and
statutory framework to argue that Congress should delay doing what needs to be
done on the premise that any problems are being handled adequately at the
administrative level.

To prevent our dialogue with you from being misinterpreted in this way, GPhA
urges FDA to issue a statement that regulatory changes, while needed, cannot
address basic problems inherent in the statutory scheme. FDA's statement should
make clear that the dialogue you have initiated cannot be, and should not be
viewed as, a substitute for needed legislative reform, or as a reason for Congress
to defer consideration of proposed legislation to achieve that goal.

We look forward to discussing the regulatory improvements described in the
attached submission.

Sincerely,

Bill Nixon

President and CEO
Overview

More now than at any time in our history, the considered attention of the public, federal and state governments, policymakers and lawmakers is focused on the price of drugs and the role and practices of America's pharmaceutical industry. Consumers increasingly bear more of the cost of their treatment. Federal and state governments, managed care companies and employers who foot the bills are trying to grapple with spiraling drug expenditures, which have jumped 92 percent in five years, to $116.9 billion, according to the Employee Benefit Research Institute.¹

We are at a critical juncture. Consumers, employers and federal and state governments now ask, "What can be done to address this pressing issue?"

One of the most immediate and significant ways to confront this issue is to encourage the sale of generic drugs by supporting a fair, balanced regulatory and statutory regime that respects the economic rights of brand-name companies while maintaining reasonable prices for drugs and thus access to affordable medicine for all citizens.

Congress endorsed this approach in 1984 when it enacted the Drug Price Competition and Patent Term Restoration Act (referred to here as the Hatch-Waxman Act or the Act). This legislation created an expedited process for generic drug applications and at the same time encouraged innovation by providing additional exclusive marketing time for brand drug products.

Hatch-Waxman was an attempt to strike a fair balance between the right of brand-name companies to obtain reasonable intellectual property protection and the societal goal of providing timely access to affordable generic drugs and improved healthcare once the NDA-holders' patents have expired.

Thus, one of the basic purposes of Hatch-Waxman was to create a regulatory environment where generic drugs could be promptly approved in a timely manner. In addition, Hatch-Waxman created an incentive to encourage generic companies to invalidate patents or innovate around them. While these goals were realized in the first decade of Hatch-Waxman, this is no longer the case. Brand-name drug companies are increasingly manipulating the Hatch-Waxman framework to improperly extend product market viability protections for their products and thereby to unduly delay the marketing of lower-cost generic medicine.

As a result of this manipulation, and in direct contravention of the goals of the Hatch-Waxman Act, generic companies are currently faced with enormous legal bills, long delays in approval and market entry, and the business uncertainty of not knowing if or when a generic drug product will enter the market. For their part, brand-name companies spend considerable resources making minor modifications to existing products to extend their monopolies. In the last few years, the pace of this distortion has increased exponentially.
Moreover, since Hatch-Waxman was enacted in 1984, several legislative enactments have tipped the balance of Hatch-Waxman in favor of brand-name companies. For example:


(2) *Uruguay Round Agreement Act*, Pub. L. 103-465, GATT, and TRIPS; and

(3) Pediatric Exclusivity provisions of the *FDA Modernization Act*, Pub. L. 105-115

Putting aside these additional obstacles, however, it bears repeating that the Hatch-Waxman system requires substantial changes. The process envisioned by Congress to ensure expedited review of generic drug applications has become anything but swift; it is no longer fair and balanced; and it serves as a means by which brand-name companies stifle natural and healthy competitive forces in the marketplace.

The Generic Pharmaceutical Association ("GPhA"), on behalf of its members and American consumers, is deeply concerned about the profound impact of brand-name drug company practices. GPhA also acknowledges that the breadth and sophistication of the brand-name tactics is beyond the ability of FDA to fully address. Both legislative and regulatory action is urgently needed to restore the balance of the Hatch-Waxman Act and the policy objectives behind it. In this submission, we will address only those changes that are within the jurisdiction of FDA, under current law.

**FDA Action Sought**

Within the existing statutory regime, FDA has the authority to pursue now the following solutions to the stated problems:

**Problem #1: Successive 30-Month Stays**

**Solution:** FDA Should Make Clear that the Hatch-Waxman Act Only Authorizes One 30-Month Stay per ANDA.

**Problem #2: Orange Book Patent Listing Abuse**

**Solution #1:** FDA Should Strengthen the NDA Holder Patent Listing Declaration.

**Solution #2:** FDA Should Use the Strengthened Declaration to Better Implement the Statutory Bar on Listing Patents.
Problem #3: Three-Year Exclusivity Can Be Misused to Block ANDA Approval.

   Solution #1: FDA Should Reaffirm that ANDA Labeling Can Omit any "Aspect of Labeling" of the Listed Drug that Is Subject to Patent or Exclusivity Protection.

   Solution #2: FDA Should Reaffirm that Exclusivity Only Be Given for Important Changes of Use.

   Solution #3: FDA Should Reaffirm that Labeling Changes for Safety and Risk Information are not entitled to Exclusivity.

Problem #4: Generic Biologics Are Not Permitted

   Solution: FDA Should Approve Generic Biologic ANDAs Under Section 505(b)(2) of the Federal Food Drug and Cosmetic Act, and Accept Paper BLAs in Support of Biologic Applications.

Problem #5: FDA Not Meeting Mandated 180-Day Period for ANDA Approval

   Solution: FDA Should Observe the Statutory Timeframe and Not Let Citizen Petitions Delay Approval.

Problem #6: False and Misleading Brand Anti-Generic Campaigns

   Solution: FDA Should More Aggressively Police False and Misleading Brand-Name Promotional Activities.

As noted above, current regulation of generic drugs is largely governed by the Hatch-Waxman Act. The Act was intended to strike a balance between the twin goals of encouraging innovation by brand-name companies and ensuring that consumers have quick and easy access to lower-cost generic medicines.

In aid of these twin goals, the Hatch-Waxman Act established a process for the listing of patents by brand-name companies and the challenging of those patents by their generic competitors. This process was designed to resolve as early as possible the respective rights of both types of drug companies.

The process was intended to work as follows. First, a brand-name company with a pending or approved new drug application (NDA) must submit information on any patent that purports to "claim" the drug that is the subject of that NDA and to which a claim of patent infringement could reasonably be asserted. 21 U.S.C. § 355(b), (c)(2). FDA publishes a list of patents that meet the statutory criteria in the list of Approved Drug Products With Therapeutic Equivalence Evaluations - commonly known as "the Orange Book."
An Orange Book listing is intended to provide generic drug companies with notice of the patents that the brand company either owns or licenses that claims the relevant NDA. The Hatch-Waxman Act then requires the generic company filing an ANDA for a particular generic drug to identify and account for each Orange Book-listed patent that protects the brand-name version of that drug. Specifically, the ANDA applicant must certify to one of the following for each Orange Book-listed patent:

(I) That the patent information has not been submitted to FDA;

(II) That the patent has expired;

(III) The date on which patent will expire; or

(IV) That the patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the product for which the ANDA is submitted.

21 C.F.R. 314.94.2

A certification by the generic company under Paragraph IV informs the brand-name company that the generic company is challenging its patent. Under the Hatch-Waxman Act, the generic company may market its product unless, within 45 days of notice, the brand-name company sues for infringement. If such a suit is filed, the Hatch-Waxman Act also provides that the brand-name company is entitled to an automatic 30-month stay of FDA's final ANDA approval, or a stay until a judicial determination of the patent dispute, whichever comes first. 21 U.S.C. § 355(j)(5)(B)(iii).3 This 30-month stay amounts to an automatic preliminary injunction against the generic company and FDA.

An Orange Book listing therefore plays a critical role in the process by which the Hatch-Waxman Act seeks to balance the interests of generic and brand-name drug companies. It is designed to "smoke out" legitimate patent disputes, so that these disputes can be resolved through early litigation and so that, if the dispute is resolved in favor of the generic company, invalid, unenforceable, or non-infringed patents do not act as an undue obstacle to the public's access to lower-priced medicines.4 Unfortunately, however, the 30-month stay provision has proven to be a powerful tool for brand-name companies, who in essence are able to receive up to two and one-half years of automatic market exclusivity as a result of an Orange Book listing.

As one court recently noted, the 30-month stay of generic ANDAs that can flow from a patent listing provides brand-name companies with "considerable incentive to cause the FDA to list patents in the Orange Book."5 This is because the 30-month stay permits the brand-name company to make monopoly profits during that period. There is no downside risk or disincentive to discourage the NDA holder from commencing litigation and obtaining the Hatch-Waxman stay. Monopoly profits during the stay period will virtually always be greater than the legal and other costs of the litigation. The continued monopoly profits are a risk-free business opportunity during the stay period.
This enormous incentive has caused brand-name companies to seek a succession of Orange Book listings in a single case in order to trigger a succession of 30-month stays of a particular ANDA. In some cases, just as patent litigation occasioned by an Orange Book listing is about to wind down, and as the 30-month stay resulting from that litigation is about to end, the brand-name company will seek an Orange Book listing of a new patent that it claims to be related to the NDA, thereby requiring the generic company to file another Paragraph IV certification, which, in turn, the brand-name companies argue, triggers another 30-month stay.

The brand-name companies' use of the Orange Book listing process to trigger what could potentially be an indefinite string of 30-month stays clearly contravenes the Hatch-Waxman Act's goal of using the Orange Book listing process to resolve expeditiously patent disputes and to ensure timely access to affordable generic medicines. The practice of seeking successive, and in some cases eleventh-hour, Orange Book listings would be bad enough if these listings conformed to the Hatch-Waxman Act's criteria for Orange Book listings - i.e., that the patent claim an approved drug and that the claim could be reasonably asserted in patent infringement litigation. To make matters worse, however, the brand-name companies, in their zeal to prevent the marketing of generic versions of their products, often seek Orange Book listings for patents that are in no way entitled to Orange Book listing under the Hatch-Waxman criteria. As previously stated, only patents that meet these criteria are eligible for Orange Book listing. FDA has generally characterized its role in reviewing requests for Orange Book listings as "ministerial," and has therefore not undertaken to review carefully whether a particular patent meets the statutory criteria for listing. Currently, FDA regulations simply require that a proponent of an Orange Book listing certify in a conclusory manner that the patent covers the formulation, composition, or use of the product described in the NDA. 21 C.F.R. 314.53(c)(1),(2). This cursory review does little to deter brand-name companies from seeking to list patents that do not meet the Hatch-Waxman Act's listing criteria.

In short, the brand-name companies are manipulating the Hatch-Waxman Act by seeking the improper Orange Book listing of patents and by using those listings to obtain an indefinite succession of 30-month stays against generic competitors.

Two other provisions of the Hatch-Waxman Act are important for purposes of this submission. First, subject to limitations in some cases, the Hatch-Waxman Act generally provides that once an ANDA has been submitted to FDA, the Agency has 180 days to approve the ANDA or to provide the ANDA applicant with an opportunity to be heard on the ANDA (assuming a 30-month stay is not in effect). 21 U.S.C. § 355(c)(1).

Second, the Hatch-Waxman Act provides for brand-name companies to obtain additional patent protection for a period of three years as a result of new clinical investigations of a drug that has already been approved by FDA. 21 U.S.C. § 355(j)(5)(D)(iv). Specifically, this provision of Hatch-Waxman grants a brand-name company the exclusive right for three years to label its product for the newly-investigated use.
Just as brand-name companies have abused the Orange Book process, they too have used both the 180-day limit on FDA approvals of ANDAs and the three-year exclusivity provisions of Hatch-Waxman to block the marketing of generic competitors.

**Problem #1: Successive 30-Month Stays**

**Brand-name drug companies have effectively used the 30-month stay provisions of the Hatch-Waxman Act to block the marketing of lower-cost generic drugs. FDA must address these abuses if the Act's overriding purposes are to be achieved.**

**Legislative Solution: McCain-Schumer Bill (S. 812)**

At the threshold, GPhA notes that there is a legislative solution to the 30-month stay problem pending in Congress. Senators McCain and Schumer have introduced S.812, the *Greater Access to Affordable Pharmaceuticals Act of 2001*, which would repeal the Hatch-Waxman Act's automatic 30-month stay provision.

Under S.812, a brand-name company may sue a generic competitor on the basis of a Paragraph IV certification and may enjoin marketing of the generic product while the lawsuit is pending if it can satisfy the test ordinarily applied by courts to determine entitlement to a preliminary injunction. S.812 treats drug patents no differently from other patents, which have never been subject to a 30-month stay.

In 1984, the supporters of the 30-month stay argued that because generic drug companies were small and essentially judgment-proof, the prospect of damages in a patent infringement action would not deter infringement by these companies. S. 812 recognizes, however, that the generic industry has matured considerably since 1984 and that, because generic companies are substantial enterprises, traditional patent law remedies are generally a significant and sufficient deterrent to infringement. In cases where this is not so, nothing in S. 812 prevents the brand-name company from petitioning the court to have a preliminary injunction entered on the basis that the brand-name company would suffer irreparable harm in the absence of a stay.

GPhA strongly supports passage of S. 812.

**Regulatory Solution: FDA Should Make Clear that the Hatch-Waxman Act Only Authorizes One 30-Month Stay per ANDA**

GPhA recognizes that the question of whether to eliminate the 30-month stay altogether is outside the purview of FDA. The Agency, however, does have the authority to address the abuses of the 30-month stay provisions by brand-name companies by making clear that the Hatch-Waxman Act does not authorize more than one 30-month stay per ANDA. As discussed above, it is the brand-name companies' efforts to use such successive stays as a means of indefinitely postponing the marketing of generic competitors that has undermined so thoroughly the intent of the Hatch-Waxman Act.
Both the text of the Hatch-Waxman Act and the legislative history of that statute make clear that the Act precludes the issuance of successive 30-month stays.

The Act's text sets forth a mandatory timetable under which FDA must issue effective approval of a generic company's ANDA that contains a Paragraph IV certification. Specifically, the Act provides that if a patent holder files an infringement action within 45 days of receipt of notice of the certification, "approval [of the ANDA] shall be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice provided under paragraph (2)(B)(i)," unless the district court makes a determination on the patent's validity before expiration of the 30-months. 21 U.S.C. § 355(j)(5)(B)(iii) (emphasis added).

Courts have repeatedly held that "the word 'shall' is the language of command in a statute." *Southwestern Bell Corp. v. FCC*, 43 F.3d 1515, 1521 (D.C. Cir. 1995) (internal citation omitted). Congress' use of the word "shall" in the Hatch-Waxman Act is a clear and unequivocal directive to FDA to make approval of an ANDA effective upon expiration of a single 30-month stay. The statute nowhere permits FDA to avoid this mandatory duty, or thereby to delay approval beyond the original 30-month period for any reason, including additional Paragraph IV certifications to subsequently-listed patents. Once FDA approves an ANDA, and once a single 30-month stay has expired, the Agency's task of making that approval effective is non-discretionary and purely ministerial.

If there is any ambiguity in the statute, it is resolved by the underlying purpose of the stay provision and its legislative history. Congress adopted the stay provision to strike a reasonable balance between the competing interests of NDA sponsors and patent holders, on one hand, and generic drug manufacturers on the other. As the House Committee on Energy and Commerce observed in 1984, allowing patent holders to sue generic drug manufacturers before the generic company begins marketing "fairly balances the rights of a patent owner to prevent others from making, using, or selling its patented product and the rights of third parties to contest the validity of the patent or to market a product which they do not believe is claimed by the patent." H.R. Rep. No. 98-857 (Part I), 98th Cong. 2d Sess. (1984) at 28. The House Judiciary Committee, which also considered the Hatch-Waxman Act, similarly stated that the stay provision:

Was added by the Committee on Energy and Commerce to accommodate the competing concerns of the [Pharmaceutical Manufacturers Association (PMA)] and the generic manufacturers. The PMA was willing to compromise on the provisions of title I of the bill (relating to abbreviated new drug application procedures (ANDAs)) in exchange for some greater protection of existing human pharmaceutical patents. The generic manufacturers, on the other hand, were willing to live with an eighteen month rule [subsequently extended to 30 months] because of other provisions of the bill.

In reaching this compromise, Congress rejected a proposed amendment that would have delayed effective approval of a generic drug until a patent had expired or a district court had made a final decision that the patent in question was invalidated, unenforceable, or non-infringed. See id. at 9. That proposed amendment was rejected because "a requirement that FDA defer generic approval until after a court decision of patent invalidity would substantially delay FDA approvals." Id. In other words, Congress determined that the objective of a final judicial resolution of patent rights should not serve as a barrier to generic drug entry into the market beyond 30 months.

As a result, Congress gave FDA no discretion to delay approval of the generic application for more than 30 months. The Committee on Energy and Commerce wrote: Once either the expiration of 30 months or the district court's resolution of the patent infringement action "occurs and the approval of the ANDA becomes effective, then the FDA has discharged its statutory responsibility with respect to making the approval of the generic drug effective." H.R. Rep. No. 98-857 (Part 1) at 27. Congress did not intend for more than one 30-month stay to delay marketing of a generic drug.

The importance of permitting only a single 30-month stay is further supported by FDA's decision to play a purely ministerial role in listing patents. FDA does not currently evaluate whether patents submitted for listing in the Orange Book qualify under the FFDCA's listing standard and, therefore, does not question whether a 30-month stay is triggered by a valid patent dispute or by a patent filed pretextually to obstruct approval of a generic drug.

If FDA declines to screen multiple listings and recognizes multiple stays, brand-name drug companies can manipulate - and, as we discuss above, have manipulated -- the 30-month stay provision by making sequential patent applications on the same drug, thereby triggering successive 30-month stays and indefinitely delaying the marketing of generic drugs.

Such a result is plainly at odds with the underlying purpose of the Hatch-Waxman Act, which was "to expedite the approval of generic versions of name-brand drugs that already have FDA approval, thus making available more low-cost generic drugs." Teva Pharmaceuticals, USA, Inc. v. FDA, 182 F.3d 1003, 1004 (D.C. Cir. 1999). See also In re Barr Labs, Inc., 930 F.2d 72, 76 (D.C. Cir. 1991) (a central purpose of Hatch-Waxman Act is to "get generic drugs into the hands of patients at reasonable times - fast").

The absence of successive 30-month stays under the Hatch-Waxman Act does not mean that brand-name companies are without protection against suspected infringers. The patentee of course retains whatever rights it has under the patent law to assert claims for infringement. And to the extent that the patentee can demonstrate to the court that it can satisfy the criteria for the award of a preliminary injunction extending the stay, the court may grant such relief. In any event, it is clear that the Hatch-Waxman Act does not provide for successive automatic 30-month stays.
Other provisions of the Hatch-Waxman Act also support limiting the number of 30-month stays per ANDA. For example, the Act specifically states that the 30-month stay runs from "the date of the receipt of the notice provided under paragraph (2)(B)(i)" - that is, the original Paragraph IV certification. 21 U.S.C. § 355((j)(5)(B)(iii). There is no similar authorization when a Paragraph IV certification is submitted to address a patent listed after an ANDA has been filed and is undergoing review. To the contrary, by specifically referring only to notices under "paragraph (2)(B)(i)", Congress expressly excluded any references to paragraph (2)(B)(ii), the separate statutory provision that requires notice of a certification added by amendment to an ANDA.

Well-established principles of statutory construction make clear that the inclusion of one item in a statutory provision means the exclusion of other unmentioned items. E.g., *Thomas v. Pierce, Hamilton & Stern*, 967 F.Supp. 507, 510 (N.D.Ga. 1997) (applying the "well-worn Latin maxim inclusio unius est exclusio alterius."). Thus, it is clear that the statute did not contemplate 30-month stays to arise out of amendments to an ANDA. FDA's own regulations confirm that fact. See 21 C.F.R. 314.95; 314.107(b)(3) (both of which fail to impose any statutory stay based on a Paragraph IV certification added by amendment). The fact that a 30-month stay cannot arise out of an amended ANDA is consistent with a determination that successive 30-month stays are impermissible under the Hatch-Waxman Act, since the original ANDA would give rise to only one 30-month stay under the statute.

In short, the text of the Hatch-Waxman Act makes clear that Congress did not intend to permit successive 30-month stays, and the statute's legislative history and purpose support this reading. Any interpretation that the statute permits such successive stays flies in the face of this clear evidence of legislative intent, and is impermissible, under recognized principles of administrative law. See *Chevron USA, Inc. v. Natural Resources Defense Counsel*, 467 U.S. 837, 842-43 (1984) ("If the intent of Congress is clear, that is the end of the matter, for the . . . agency . . . must give effect to the unambiguously expressed intent of Congress.")

GPhA urges FDA to give effect to Congress' clearly expressed intent that an ANDA be made effective after the expiration of a single 30-month stay. GPhA recognizes that the Agency has taken the position in litigation that successive 30-month stays are permissible under the Hatch-Waxman Act. However, the Agency's regulations do not address this issue and we urge FDA to reconsider its litigation position in light of the compelling evidence of Congress' contrary intent.

Agency guidance on this issue should be unnecessary, given the clearly-expressed intent of Congress. However, in light of the frequency with which such successive stays have been sought by brand-name companies in patent infringement cases, it is essential that FDA provide clear and comprehensive direction on this important question. In this regard, GPhA believes an Industry Guidance would be sufficient for this purpose, and that such Guidance can and should be issued expeditiously.

**Problem #2: Orange Book Patent Listing Abuse**
NDA holders have submitted patents for listing in the Orange Book that do not comply with the statutory requirement for listing.

The Federal Food Drug and Cosmetic Act ("FFDCA") provides the starting point for the determination of what kind of patents should be listed in the Orange Book. The Act's provisions regarding submission and listing patents are explicit and unambiguous. 21 U.S.C. § 355(b) requires the NDA applicant to submit patent information on any patent:

which claim[s] the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use or sale of the drug

(Emphasis added). Further, 21 U.S.C. § 355(c)(2), which provides for the submission of patent information on patents that issue after an NDA has been approved, states:

If the patent information described in subsection (b) of this section could not be filed with the submission of an application under subsection (b) of this section because...a patent issued after the application was approved...the holder of an approved application shall file with the secretary the patent number and expiration date of any patent which claims the drug for which the application was submitted...(Emphasis added)

Finally, the FFDCA prohibits the listing of process patents. 21 U.S.C. § 355(b)(1); 21 C.F.R. 314.53(b).

As discussed above, the Orange Book listing process is critical to the Hatch-Waxman framework, because it triggers (1) the ANDA applicant's requirement to certify to the listed patent; and (2) if the certification is a Paragraph IV certification, the ability of the patent holder to sue and obtain the benefit of a 30-month stay.

The prospect of receiving the initial stay, combined with FDA's current policy permitting successive 30-month stays, provides brand-name companies with an enormous incentive to submit patents for listing in the Orange Book, even if the patents do not satisfy the listing criteria contained in the Hatch-Waxman Act. As a result, brand-name companies frequently abuse the patent listing provisions of the FFDCA.

The law is clear: patents that do not meet the Hatch-Waxman Act's listing criteria are not eligible for listing in the Orange Book. See Pfizer v. FDA, 753 F. Supp. 171 (D. Md. 1989). It is also clear, however, that FDA has proven reluctant to look beyond the information submitted by the brand-name proponent of the Orange Book listing in order to determine whether a particular patent should be listed. This makes the declaration provided by the NDA holder critical to ensuring the appropriateness of a patent proposed for listing.
Under current FDA practice, for FDA to agree to list the patent, a company may simply certify in the vaguest possible manner that its patent meets the Orange Book criteria. See, e.g., March 26, 2001 Letter from Eugene Melnyk, Biovail Laboratories, Inc., to the Center for Drug Evaluation and Research at FDA (declaring that U.S. Patent No. 6,162,463 meets the criteria for an Orange Book listing). See also 21 C.F.R. 314.53(c)(1), (2) (setting forth text of required declaration and other requirements for Orange Book listing submission). This lack of scrutiny has led to abuse of the Orange Book system, and to the undermining of the fundamental goal of the Hatch-Waxman Act - that is, to "get 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).

GPhA is aware of FDA's reluctance to go beyond the patent information submitted by the proponent of an Orange Book listing, and to keep its role in the Orange Book process as "ministerial" as possible. At the same time, however, the Agency has a statutory duty to ensure that only patents eligible for listing under the Hatch-Waxman Act are in fact listed. Since generic applicants have no cause of action to sue the NDA sponsor to compel delisting, enforcement of the statutory requirements is dependent on FDA.12 Moreover, the task of determining whether listing is appropriate is not a question of patent validity or patent infringement. Rather, it is a question of whether the patent meets the listing criteria set forth in a statute whose enforcement is squarely within FDA's jurisdiction. FDA has at various times suggested that it is up to the courts, and not the Agency, to determine that an Orange Book listing is inappropriate. However, the courts themselves have suggested to the contrary. See, e.g., Andrx Pharmaceuticals, Inc., v. Biovail Corp., No. 01-6194-CIV-DIMITROULEAS (S.D. Fla. March 6, 2001), Omnibus Order, at 9 ("It is the FDA's job to determine whether to list or delist a patent."). It is therefore incumbent on FDA to ensure compliance with the listing requirements of the Hatch-Waxman Act.

GPhA suggests that this process can involve two steps. The first places the burden of establishing Orange Book eligibility where it belongs - with the company seeking the listing, which is in the best position to describe the subject patent. The second requires FDA to review the information provided by the listing proponent, but not to undertake an independent review of the patent.

Solution #1: FDA Should Strengthen the NDA Holder Patent Listing Declaration

Under current FDA practice, an NDA holder submitting a patent for Orange Book listing need only declare, without explanation or detail, that its patent "covers" an approved drug and therefore meets the Hatch-Waxman criteria for Orange Book listing. This inadequate procedure for an Orange Book listing has led to FDA's acceptance for listing of numerous patents that in fact claim, for example, unapproved drugs, or unapproved uses of approved drugs, or that simply claim a different process for making an old drug - all in direct contravention of the Hatch-Waxman Act.
GPhA proposes that the current declaration requirements be strengthened to require the NDA holder to explain in detail why a submitted Orange Book listing is consistent with Hatch-Waxman and other statutory criteria. These changes to the current process would require FDA to amend its regulations, which currently set forth the patent information that Orange Book listing proponents must provide to the agency. 21 C.F.R. 314.53(c). GPhA urges FDA to make these regulatory changes on an expedited basis.

Specifically, *inter alia*, the NDA holder submitting an Orange Book listing should be required to specify to FDA the following information for each patent for which an Orange Book listing is sought:

1. The name of the patent owner (as under current law (21 C.F.R. 314.53(c)(1)(iii));
2. The patent number and expiration date (as under current law (21 C.F.R. 314.53(c)(1)(i));
3. For each patent, identify each claim that meets the statutory requirements (21 U.S.C. § 355(b), (c)(2));
4. For each claim identified in 3 above:
   - the type of claim (i.e., composition of matter, method of use, article of manufacture, or process) (as under current law (21 C.F.R. 314.53(c)(1)(ii));
   - a statement of the basis for concluding why each claim meets the statutory requirements; and
   - the earliest effective U.S. filing date(s) to which each claim of the patent is entitled.
5. Additional information as appropriate.

The declaration should also include a certification that the above information is submitted under penalty of perjury, in accordance with the requirements of 28 U.S.C. § 1746. Further, the declaration should be made publicly available at the time of listing.

FDA should then require the submission of a completed declaration as a condition for listing of a patent, and should refuse to list a patent referred to in an incomplete declaration. If the completed declaration is not submitted within 30 days of the patent's issuance, in accordance with current regulations, FDA should treat the patent as "late-listed." *See* 21 C.F.R. 314.53 (c)(2)(ii) (setting forth 30-day rule). In any event, the date of listing cannot be earlier than the date of the submission of a complete declaration. The information contained in this strengthened declaration will enable FDA to satisfy its current statutory obligations.
Solution #2: FDA Should Use the Strengthened Declaration to Better Implement the Statutory Bar on Listing Patents

The mere fact that an Orange Book listing proponent would be required to explain in detail the basis for the requested Orange Book listing would, standing alone, go a long way toward enforcing the requirements of the Hatch-Waxman Act. The requirement of a detailed and substantive declaration, combined with a strong anti-perjury provision, would serve to deter wrongdoing and would force brand-name companies to consider carefully whether a given patent is entitled to be listed in the Orange Book.

GPhA submits, however, that the strengthened declaration could also serve as the basis for FDA to undertake a limited substantive review of the Orange Book issues related to the patent, and to refuse to list a patent that does not meet the statutory criteria. GPhA acknowledges FDA's concern about undertaking a full investigation of all patents submitted for listing. But a more detailed declaration obviates much of the need for such a full investigation. The information submitted to FDA by the expert on the particular patent, i.e., the party seeking the listing, will provide the Agency with much, if not all, of the information it needs to ensure strict compliance with the requirements of the Hatch-Waxman Act.

The information that GPhA proposes be submitted to FDA as part of an Orange Book submission will assist the Agency's listing determination in the following ways.

A. The Declaration Would Reveal Whether the Patent Claimed the FDA-Approved Drug in All Respects

The strengthened declaration would require the Orange Book listing proponent to set forth in detail (1) the approved drug or method of use that the patent claims, (2) the basis on which the Orange Book proponent could sue for infringement of that patent, and (3) the connection between the approved product or method of use that forms the basis for the Orange Book listing and these patent infringement claims. These statements would therefore enable FDA to determine upon a mere review of the declaration whether the patent submitted for listing met the Hatch-Waxman criteria for listing - i.e., that (1) the patent claims an approved drug in all respects14 (21 U.S.C. § 355(b)(1), (C)(2)); and (2) that the claim on which the patent is based must be one that "could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, sale, or use of the drug." Id.

The effect of the new declaration would be that it would no longer be possible for a proponent of an Orange Book listing to state in a conclusory manner that the patent meets the Hatch-Waxman criteria. Rather, the proponent would have to demonstrate that this is so, and further to show that any infringement claims it might have on the new patent could be traced back to the approved drug product (or approved method of use). This information, in turn, would allow FDA to assess the propriety of an Orange Book listing under the Hatch-Waxman Act without having to go beyond the submission of the listing proponent.
B. The Declaration Would Reveal Whether the Patent Was a Process Patent, Which is Ineligible for Orange Book Listing

The Hatch-Waxman Act on its face prohibits the listing of process patents. 21 C.F.R. 314.53(b) ("process patents are not covered by this section and information on process patents may not be submitted to FDA"). Requiring an Orange Book proponent to list the kind of patent claim in the Orange Book declaration would enable FDA to determine whether the patent was a process patent, and therefore ineligible for Orange Book listing.

A particular type of process patent that is frequently listed in the Orange Book, and that a strengthened declaration would expose, is the so-called "product-by-process" patent. A legitimate product-by-process patent contains claims which describe a product that can only be described with reference to a particular process, and not with reference to the physical or chemical properties of the compound or its structural formula. But many product-by-process patents, like simple process patents, in fact simply claim a process because it cannot claim any new chemical compound that was not already the subject of a prior patent. If such a patent is allowed to be listed, it enables the listing proponent to extend protection of the product based on nothing more than a change in the process by which the product was made. Listing of a product-by-process patent, like the listing of a process patent, runs against the Hatch-Waxman Act's goal of using Orange Book listing as an incentive for companies to develop new products, not new processes.

Product-by-process claims appear in various factual situations, including:

· Where the product is novel and inventive, but cannot be described other than by the process (this is very rare for pharmaceutical inventions, which can generally be described in terms of their chemical structure); and

· Where the product is not new, but there is a novel process-based limitation.

In addition to an NDA holder's patent covering the basic compound, a patentee may have several product-by-process patents listed in the Orange Book. These patents assert claims to processes for the manufacture of a particular product but do not claim any new compound not previously the subject of a prior patent. In this way, a patentee is able to extend their scope of protection, requiring the generic to address all listed patents. Under current FDA practice the presence of these patents in the Orange Books leads to multiple 30-month stays for brand-name companies.

From FDA's perspective, the validity of these patents is not an issue - the PTO has issued the patents and they must be presumed to be valid. The relevant question is whether these types of patents are consistent with the statutory prohibition on listing process patents, and whether they should be listed in the Orange Book, leading potentially to a 30-month stay.

As a matter of policy, it would not be contrary to the public interest to allow true product-by-process claims where the inventor cannot describe the product in ordinary terms.
However, for pharmaceutical products, there is no reason in the vast majority of cases why the product could not be described in terms of the structural formula or the physical or chemical properties such as melting point, crystal structure, and pH. In fact, most patents covering active ingredients are expressed in terms of structural formula.

In spite of the PTO's statements on patentability, most pharmaceutical product-by-process patents in fact do not describe a new substance, but rather cover the old substance made by a new process.

It is clear that the Hatch-Waxman Act was not meant to cover process patents; it is equally clear that most product-by-process patents are no more than process patents that are ineligible for Orange Book listings. Patentees should not be able to enforce successive 30-month stays by virtue of having more than one patent with claims to the active compound. Accordingly, FDA should refuse to list product-by-process patents where there is already a patent covering the active ingredient. This position does not limit the rights ordinarily available to a patentee. Removing product-by-process patents from the Orange Book does not take away the patentee's ability to sue for patent infringement if the generic manufacturer is using the patented process; it merely removes the extra barriers to generic market entry created through the Orange Book listing and the 30-month stay.

The strengthened patent declaration will enable FDA to identify product-by-process patents that claim nothing more than a change in process, and whose listing runs counter to the goals of Hatch-Waxman.

**Problem #3: Three-Year Exclusivity Can Be Misused to Block ANDA Approval**

*Brand-name companies also seek to abuse the Hatch-Waxman Act by attempting to block the marketing of generic drugs via the statute's three-year exclusivity provision. 21 U.S.C. § 355(j)(5)(D)(iv).*

The three-year supplemental NDA provisions, 21 U.S.C. § 355(j)(5)(D)(iv), enables brand-name companies that have conducted new clinical investigations that support Supplemental NDA approval to enjoy a three-year exclusive right to the application's change. In many instances, the application's change concerns a modification to the product's labeling which is confirmed or discovered during these new clinical investigations. These labeling changes range from important innovations, such as a novel therapeutic indication of use, to less meritorious changes, such as a clarification of a titration method. Yet the congressional intent of this provision was to reward *important, innovative* changes, not minor product changes. For example, if a supplemental NDA provides for a new pediatric or geriatric use of the drug, the brand-name company submitting the supplemental NDA is entitled to exclusively market the drug for this new pediatric or geriatric use for three years.
Moreover, brand companies not only seek three years of exclusivity for minor product changes, but also have sought to expand the reach of this limited provision by arguing that any three-year exclusivity period provided under the statute acts to completely block the approval and marketing of the generic version of the brand drug, not just to prevent the labeling of the generic for the particular use that gives rise to the exclusivity.

In making this argument, some brand-name companies have relied on the provision of the Hatch-Waxman Act that states that a generic label must be "the same" as the brand-name label. 21 U.S.C. § 355(j)(2)(A)(v). If a brand-name company enjoys three-year exclusivity, they argue, the generic drug's labeling will not include the new use or an aspect of the labeling protected by the exclusivity, which means that its labeling is not "the same" as the brand-name drug's labeling and that, therefore, the generic drug cannot be marketed at all. If accepted, this argument would deprive the consumers of access to lower cost generic drugs, thus raising health care costs and restricting many citizens from access to critically-needed medication.

Legislation signed into law by the President just weeks ago has resolved this issue in favor of the generic drug companies in the pediatric context. See Pub. L. 107-109 (January 4, 2002) (making clear that any three-year exclusivity based on pediatric labeling statements of an approved drug serves only to prevent generic versions of the drug to claim the pediatric statement on the label, not to block the marketing of the generic drug in its entirety).

While the recently-passed legislation codifies FDA's regulations permitting labeling carve-outs as well as FDA's authority to provide pediatric alternative labeling statements, the legislation does not address exclusivities in the non-pediatric context. FDA and the courts have consistently taken the position that the three-year exclusivity cannot be used to block the approval and marketing of generic drugs. But the brand-name companies will undoubtedly argue that the limited scope of the legislation reflects Congress' intent that the three-year exclusivity be used to block the marketing of generic drugs in non-pediatric contexts. Thus, FDA must reaffirm its position regarding the scope of the three-year supplemental exclusivity and its view that Congress did not intend that provision to block the marketing of generic drugs.

Solution #1: FDA Should Reaffirm that ANDA Labeling May Omit Any "Aspect of Labeling" of the Listed Drug that Is Subject to Patent or Exclusivity Protection

Current FDA regulations make clear that the label of a generic drug may differ from that of the brand-name version of the drug where the differences are due to exclusivities enjoyed by the latter. See 21 C.F.R. 314.94(a)(8)(iv) ("[D]ifferences between [a generic applicant's] proposed labeling and labeling approved for the [innovator drug] may include . . . omission of an indication or other aspect of labeling protected by patent or accorded exclusivity under section 505(j)(5)(D) of [the Hatch-Waxman Act]" (emphasis added). See 21 U.S.C. § 355(j)(2)(A)(viii); see also 21 C.F.R. 314.127(a)(7) (permitting differences in generic and innovator labels where "aspects of the listed drug's labeling are protected by patent, or by exclusivity, and such differences do not render the proposed
drug product less safe or effective than the listed drug for all remaining, non-protected conditions of use.").

The courts have upheld FDA's regulations against the challenge that they are inconsistent with the Hatch-Waxman Act's requirement that the generic and innovator label be the same - precisely the argument that the brand-name companies continue to make. *Bristol-Myers Squibb Co. v. Shalala*, 91 F.3d 1493 (D.C. Cir. 1996); *see also Zeneca v. Shalala*, 1999 U.S.Dist. LEXIS 12327, *31-34 (D.Md. August 11, 1999), affirmed 213 F.3d 61 (4th Cir. 2000) (upholding FDA's approval of generic drug that contained different labeling from innovator drug because of three-year exclusivity).

In *Bristol-Myers*, the D.C. Circuit relied on the language in the Hatch-Waxman Act that permitted differences in the generic and innovator labeling where "the new drug and the listed drug are produced or distributed by different manufacturers." 91 F.3d at 1500 (citing 21 U.S.C. § 355(j)(2)(A)(v)). The court also noted that the FDA's interpretation of the three-year exclusivity provision "finds unusually strong support in the legislative history of the [the Hatch-Waxman Act]," which reflected Congress' intent that an ANDA could "be approved for less than all of the indications for which the listed drug has been approved." *Id.* at 1500, quoting H.R. Rep. No. 857 (Part I), 98th Cong., 2d Sess. 21-22, reprinted in U.S.C.C.A.N. 2654-55. Finally, and most importantly, the D.C. Circuit pointed out that the brand-name companies' reading of the three-year exclusivity provision was simply inconsistent with the amount of protection Congress sought to provide these companies:

The appellant's interpretation of [Hatch-Waxman three-year exclusivity] . . . would turn [it] into a bar to the generic manufacturer's use of research undertaken to obtain approval for *any* indication for the pioneer drug, a reading that offers much broader protection from competition that [the exclusivity provisions] would otherwise offer. *Id.*

The D.C. Circuit Court's *Bristol-Myers* decision demonstrates that FDA stands on firm ground when it prevents the three-year exclusivity from being used to prevent the marketing of certain generic drugs altogether. The Agency should not stray from its past reading of the statute, and should issue an industry guidance clarifying once again its view of the limits of three-year exclusivity.

**Solution #2: FDA Should Reaffirm that Exclusivity Only Be Given for Important Changes of Use**

In recognizing that there are statutory limitations on the three-year supplemental exclusivity provision, FDA has unequivocally stated that the provision is intended to reward NDA sponsors for conducting investigations "necessary for approval of important innovations requiring substantial study, such as significant new therapeutic uses." 54 Fed. Reg. 28872, 28899 (July 10, 1999) (proposed regulation). The Agency has stated that these exclusivities should not be granted for "any change to an approved drug" merely because it reflects the results of a clinical investigation. 59 Fed. Reg. 50338, 50356-57 (Oct. 3, 1994) (final regulation). Despite these clear and reasonable limitations on the
scope of the three-year exclusivity, brand-name companies have asserted their right to the exclusivity based on changes to the approved drug that in no way amount to an "important innovation[] requiring substantial study."

FDA should reaffirm its position regarding the kinds of changes that give rise to three-year exclusivity under the Hatch-Waxman Act. The requirement that the change must be an important innovation to trigger the exclusivity is consistent with congressional intent that the three-year exclusivity be awarded only in exceptional cases. It also prevents brand-name companies from using minor changes to an approved drug to limit the use or availability of lower-priced generics.

FDA should clarify in a detailed industry guidance the conditions for qualifying for the three-year exclusivity. Specifically, the Agency should set forth what it views as the kinds of "important" innovative changes that warrant this exceptional reward.

**Solution #3: FDA Should Reaffirm That Labeling Changes For Safety And Ask Information Are Not Entitled To Exclusivity**

FDA has also made clear that certain kinds of labeling changes, even though concededly important, were not intended by Congress to give rise to three-year exclusivity. For example, FDA has stated that labeling changes that involve "warning or other similar risk information" do not qualify for 3 year exclusivity.18 Because of the profound public policy implications of this issue, FDA should reaffirm in the Industry Guidance proposed in Solution #2, above, that these changes cannot serve as the basis for Hatch-Waxman three-year labeling exclusivity.

**Problem #4: Generic Biologics are Not Permitted**

Current FDA Regulations Prohibit the Approval of Generic Biologics. 21 C.F.R. § 314.101(e)(1). The Agency Should Revisit This Position.

Solution: FDA Should Approve Generic Biologic NDAs under Section 505(b)(2) of the FFDCA and Accept Paper BLAs in Support of Biologic Applications.

FDA has ample authority to approve generic biopharmaceuticals under section 505(b)(2) of the FFDCA. 21 U.S.C. § 355(b)(2).19 This section gives FDA the authority to approve drug products based on published literature and/or information contained in approved applications. As noted in Section 123(g) of the FDA Modernization Act (Pub. L. 105-115), biologics are "drugs" which are subject to regulation under the FFDCA. The current statutory language, therefore, provides FDA with ample authority to approve a 505(b)(2) NDA for a generic biologic (i.e., "drug") product based on a determination that it is comparable to an approved brand product. Accordingly, GPhA urges FDA to deny the Citizen Petition submitted by Pharmacia and Pfizer July 30, 2001 and reaffirm the concept that 505(b)(2) ANDAs are appropriate for generic biologic products.
Furthermore, GPhA urges FDA to adopt procedures enabling a manufacturer to obtain Agency approval of a generic biologic where the innovator is subject to licensure under section 351 of the Public Health Service Act (PHSA) (42 U.S.C. § 262) by submitting articles and pivotal studies demonstrating the safety and efficacy of its product. This practice would mirror the "paper NDA" procedures which the Agency applied to generic drugs prior to 1984, and that have been codified in the Hatch-Waxman Act. Currently, the biologic license application ("BLA") process is governed exclusively by section 351 of the PHSA. FDA should amend its regulations to state that this process does not preclude the approval of a generic biologic based on a "paper BLA" submission similar to the pre-1984 procedures used for generic drugs.

Congress clearly contemplated FDA's review and approval of "paper BLA" submissions when it directed FDA in Section 118 of the FDA Modernization Act to issue "a guidance that describes when abbreviated study reports may be submitted, in lieu of full reports, . . . with a [BLA] under section 351 of the Public Health Service Act . . ." In addition to clarifying that such paper BLA submissions may form the basis for the approval of generic biologics, the Agency should also issue a guidance stating the kinds of information that should be part of such a submission.

Lastly, where the science and technology have advanced to the point where compatibility can be scientifically established, FDA could and should make a therapeutic equivalence determination for each approved "generic" biopharmaceutical subject to a 505(b)(2) NDA or to "paper BLA." FDA has historically made drug therapeutic equivalence determinations as a "service" to the medical community and the States. There is, therefore, no reason why FDA could not provide its opinion on whether a generic biopharmaceutical is interchangeable with its brand-name counterpart.

**Problem #5: FDA Is Not Reviewing ANDAs Within the 180-Day Period**

The Hatch-Waxman Act states unequivocally that within 180 days of the submission of an ANDA, FDA shall either approve the ANDA or give the applicant an opportunity for a hearing on whether the ANDA can be approved. 21 U.S.C. § 355(c)(1). FDA is doing neither.

**Solution: FDA Should Observe the Statutory Timeframe for Reviewing ANDAs and Not Let Citizen Petitions Delay Approval**

There appear to be two reasons for the Agency's failure to meet its statutory duties. First, the Agency is simply failing to observe the statutory timeframe. Second, brand-name companies, in yet another example of their abuse of the current system, have taken to filing eleventh-hour citizen petitions with the Agency setting forth myriad objections to the pending ANDA, and thereby delaying FDA's review of the application.

The Hatch-Waxman Act's 180-day timeframe is unequivocal, and an ANDA applicant is entitled to the Agency's strict adherence to this timeframe. Thus, GPhA urges FDA to
strictly observe the 180-day deadline set forth in Hatch-Waxman. To the extent that brand-name companies attempt to disrupt the statutory timeframe through the filing of last-minute citizens petitions, we urge FDA to issue a guidance making clear that the filing of such a petition will not operate to stay consideration of the an ANDA beyond the statutory deadline.

Problem #6: False and Misleading Brand Anti-Generic Campaigns

Certain brand-name companies have been engaged in promotional campaigns that feature false and misleading statements about certain generic companies and generic drug products.

Solution: FDA Should More Aggressively Police False and Misleading Brand-Name Promotional Activities

For example, AstraZeneca conducted a sustained promotional campaign alleging that generic propofol was "not safe or effective, not stable, not as cost-effective as [AstraZeneca's] Diprivan, or not therapeutically equivalent to Diprivan," despite the fact that FDA had assigned the generic product an "AB" rating. See FDA Warning Letter to AstraZeneca (Sept. 1, 2001). See also FDA Warning Letter to Zeneca Pharm. (Mar. 23, 1999). Similar examples include Novartis' activities promoting Neoral (cyclosporin) (see FDA Warning Letter to Novartis Pharm. Corp. (May 8, 2000)) and DuPont Merck's campaign against generic warfarin sodium (see FDA "Untitled Letter" to DuPont Merck Pharm. Co. (Aug. 26, 1997)). These claims are without basis.

The FFDCA deems to be misbranded any drug whose labeling "is false or misleading in any particular." 21 U.S.C. § 352(a) (emphasis added). See United States v. Ninety-Five Barrels of Alleged Apple Cider Vinegar, 265 U.S. 438, 443 (1924) (discussing FFDCA's predecessor statute) ("[the statute's] comprehensive terms condemn every statement, design or device which may mislead or deceive" (emphasis added)). Thus, to the extent that a brand-name drug is found to contain labeling that contains false or misleading labeling regarding a generic competitor, it falls within the scope of the FFDCA's misbranding provisions and must be removed from the market. Yet, in reality, brand-name companies that make such misleading claims typically only receive a warning letter, if that. GPhA urges FDA to act promptly against any brand-name manufacturer found to be involved in false and misleading anti-generic promotional campaigns, and to require affirmative remedial actions to correct the misinformation or material omissions via "Dear Doctor" letters or similar submissions. Repeat offenders should be subject to stronger enforcement actions in order to preserve the system of fair competition that the FFDCA in general and the Hatch-Waxman Act in particular are designed to advance.

In conclusion, FDA has an important role in ensuring access to affordable pharmaceuticals.

For the foregoing reasons, FDA should:
(1) Make clear that the Hatch-Waxman Act only authorizes one 30-Month stay per ANDA;

(2) Strengthen the NDA holder Patent Listing Declaration and use the strengthened declaration to better implement the statutory bar on listing patents;

(3) Reaffirm that ANDA labeling may omit any "aspect of labeling" of the listed drug that is subject to patent or exclusivity protection;

(4) Reaffirm that three-year exclusivity should only be given for important changes of use;

(5) Reaffirm that labeling changes for safety and risk information are not entitled to three-year exclusivity;

(6) Approve generic biologic NDAs under section 505(b)(2) of the FFDCA or accept paper BLAs in support of biologic applications;

(7) Observe the 180-day statutory timeframe for reviewing ANDAs and not let Citizen Petitions delay approval;

(8) More aggressively police false and misleading brand-name promotional activities.


2 Generic companies have an incentive to undertake the cost of challenging patents because the Hatch-Waxman Act provides that a "patent-busting" generic company is entitled to 180 days of its own market exclusivity, during which time FDA may not approve another ANDA seeking a Paragraph IV certification for the same drug. 21 U.S.C. § 355(j)(5)(B)(iv).

3 The statute contains one express exception to this mandatory feature of the Hatch-Waxman Act, for cases when the district court hearing the patent infringement action shortens or lengthens the 30-month stay period because "either party to the action failed to reasonably cooperate in expediting the action." 21 U.S.C. § 355(j)(5)(B)(iii).


10 The original bill considered by the House Committee on Energy and Commerce provided a shorter stay of 18 months. Congress later extended the stay provision to 30 months. That Congress devoted such attention to the length of the stay is telling. If successive stays were permissible under the Hatch-Waxman Act, the length of any particular stay would be unimportant.


12 Generic applicants, however, may see under the Administrative Procedure Act to force FDA to follow statutory requirements. GPhA is aware of the recent decision of the United States Court of Appeals for the Federal Circuit, Biovail Laboratories et al., v. Andrx, No. 01-1650, 02-1025 (Fed. Cir.), released on January 17, 2002. If necessary, the decision will be addressed in GPhA's reply brief.

13 Of course, there is still the possibility that an Orange Book NDA holder will attempt to abuse the process by providing FDA with false information in its listing application. 18 U.S.C. § 1001, however, criminalizes the submission of false statements to the United States. FDA's vigorous use of this statutory provision against companies that might attempt to abuse the new certification process would go a long way toward ensuring that the Agency receive accurate and useful information through that process.

14 The same point has been made by the Federal Trade Commission in a Citizen Petition to FDA ("we read this provision [21 C.F.R. 314.53(b)] to require that after a drug is approved, a listed patent must claim the drug product approved by the FDA in all respects"). FTC Citizen's Petition to FDA dated May 29, 2001, FDA Docket No. 01P-0248.

15 The Patent Act does not address product-by-process claims directly, but does provide that patents can be obtained for "any new and useful process, ... or composition of matter". Patents are to be granted for new inventions only, that meet the statutory criteria
of novelty. (35 U.S.C. §102). The Patent Act requires the applicant for a patent to "particularly point out and distinctly claim" the invention (35 U.S.C. §112). This can include defining a product by the method of obtaining it, where the new compound cannot be defined in other ways.

16 The legislative history of the Hatch-Waxman Act confirms this interpretation. See 130 Cong. Rec. H9124 (Statement by Rep. Waxman)("This protection for three years will apply for any company, big or small, that puts in money as an investment to develop a product that will have to be approved by FDA and requires clinical tests, which means it is not just some minor change in a chemical entity that has already been approved, but a change that is significant enough to require clinical tests") (emphasis added); Id. at H9114 (noting that 3-year exclusivity "will encourage drugmakers to obtain FDA approval for significant therapeutic uses of previously approved drugs") (emphasis added); 130 Cong. Rec. S10505 (Statement by Sen. Hatch)(3-year exclusivity intended to cover changes "which require considerable time and expense in FDA required clinical testing") (emphasis added).

17 The D.C. Circuit also suggested that what Congress was particularly concerned about was whether the generic drug was safe and effective for its labeled indications of use, implying that under the Hatch-Waxman Act, a generic company could omit "any aspect of labeling", not just a "use," provided that the generic remains safe and effective for all its labeled indications. 91 F.3d at 1500.


19 GPhA is also of the opinion that FDA has the authority to approve generic biologics under section 505(j) (21 U.S.C. § 355(j)) when bioequivalence and sameness are established.