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Food and Drug Administration
5630 Fishers Lane
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Rockville, Maryland 20852

Re: 180-Day Exclusivity for ANDA 76-052

Reply to the FTC's Response to
Citizen Petition – Dkt. 2005P-0008

By letter dated April 5, 2005, the Federal Trade Commission (FTC) submitted a response to the pending citizen petition dated January 5, 2005, from IVAX Pharmaceuticals, Inc. (IPI). The IPI petition requests the Food and Drug Administration (FDA) to give effect to IPI's eligibility, under the Federal Food, Drug, and Cosmetic Act (FDCA) and 21 C.F.R. § 314.107(c), for 180-day exclusivity for four of the five strengths of simvastatin tablets. IPI's eligibility for 180-day exclusivity is based on paragraph IV certifications to the '481 and '520 patents listed by Merck & Co., Inc. (Merck), the NDA holder for Zocor, the reference listed drug. FDA has granted Merck's request to delist the '481 and '520 patents from the Orange Book.

FDA's action is based on a policy under which NDA holders are not allowed to delist paragraph IV patents on which they have sued for infringement but are allowed to delist paragraph IV patents on which they have not sued for infringement. The sole reason for maintaining paragraph IV patent listings in the circumstances at issue is to protect a first ANDA applicant's eligibility for 180-day exclusivity. Therefore, FDA's policy of allowing NDA holders to delist patents on which infringement lawsuits have not been brought imposes an unlawful condition on the eligibility of ANDA applicants for 180-day exclusivity.

By allowing Merck to delist the '481 and '520 patents, FDA has signified that it will deny 180-day exclusivity to IPI's ANDA for simvastatin tablets. The IPI petition asks FDA to

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reverse that decision, to give effect to IPI's right to 180-day exclusivity under the FDCA and 21 C.F.R. § 314.107(c), and to make clear it will do so by reinstating the '481 and '520 patent listings.

The FTC's response recommends that IPI's petition be denied on the following grounds: 180-day exclusivity is not a right but an incentive to challenge weak patents or make noninfringing formulations; Orange Book patent listings have led to anticompetitive abuses and therefore NDA holders should be allowed to delist them; and 180-day exclusivity delays generic drug competition.

IPI respectfully disagrees with the reasons for the FTC's recommendation. The FTC's argument that 180-day exclusivity cannot be a right because it is an incentive is fallacious. Incentives and rights are not mutually exclusive categories. A government patent is an incentive to invent. It is also a right that can be legally enforced in court against those who infringe it. In fact, the value of an incentive depends on the extent to which it can be enforced as a right rather than be arbitrarily denied or revoked.

An ANDA applicant legally qualifies for the incentive of 180-day exclusivity if it submits a substantially complete ANDA with a paragraph IV certification before other paragraph IV ANDAs. Responding to that incentive, IPI submitted its paragraph IV ANDA for simvastatin tablets. IPI therefore has a statutory right, enforceable in court, to remain eligible for 180-day exclusivity. FDA has violated that right.

Although the Hatch-Waxman system may be vulnerable to abuse, FDA's policy does not address the problem. The FTC's 2002 study, Generic Drug Entry Prior to Patent Expiration (Study), determined that delayed generic drug market entry occurs routinely when NDA holders sue on paragraph IV patents, but has never occurred in the absence of patent infringement litigation. FDA's policy, however, prohibits NDA holders from delisting litigated patents while allowing them to delist the ones on which no litigation is brought and which are therefore causing no delay – the exact opposite of what the FTC's own study would seem to call for.

In any event, delays in generic drug market entry have not resulted from questionable Orange Book patent listings. They have resulted from lawsuits brought by NDA holders in response to paragraph IV notices, which trigger automatic 30-month stays of ANDA approval. NDA holders that file lawsuits will obviously not delist the patents on which those lawsuits are based. Conversely, NDA holders willing to delist patents voluntarily, as provided in FDA's policy, can avoid delaying generic competition just as effectively by leaving the patents in the Orange Book and voluntarily not filing infringement lawsuits. Therefore, FDA's policy of allowing NDA holders to voluntarily delist patents that are not the subject of infringement lawsuits is not necessary for the purposes the FTC believes it serves. Instead, the policy serves only the purpose of denying 180-day exclusivity to eligible ANDA applicants, and doing so, not by applying objective standards, but by granting NDA holders' unilateral and unexplained decisions to remove patents from the Orange Book. FDA's policy thus creates additional opportunities for anticompetitive manipulation of the Hatch-Waxman system rather than reducing them.

The FTC's assertion that granting the IPI petition will adversely affect generic drug competition focuses on the 180-day period during which only the first applicant may market a generic version of the brand drug. Overlooked by the FTC response is that the prospect of exclusivity to the first applicant encourages earlier submission of all ANDAs for the brand product, leading to unrestricted generic competition sooner than it would otherwise occur even after taking the 180-day exclusivity period into account. Contrary to the FTC's response, therefore, 180-day exclusivity produces a net increase in generic drug competition.

Ultimately, the FTC's submission is irrelevant to the IPI petition. The IPI petition objects only to FDA's disparate treatment, within the Hatch-Waxman rules, of ANDAs with paragraph IV certifications that lead to infringement lawsuits and those that do not. In comparison, the FTC's arguments – 180-day exclusivity is not a right, NDA holders must be allowed to "correct" the Orange Book, 180-day exclusivity reduces competition – apply as much to 180-day exclusivity based on paragraph IV certifications that result in patent infringement lawsuits as

they do to 180-day exclusivity in which there is no lawsuit. The FTC's criticisms, therefore, are aimed not at the IPI petition but at the Hatch-Waxman Act as interpreted by FDA and the courts.

1. Mova and § 314.107(c) establish IPI's right to exclusivity.

The FTC response does not address the central point of IPI's petition. The rule against delisting a patent in § 314.94(a)(12)(viii)(B) is the means for giving effect to 180-day exclusivity under § 314.107(c). Therefore, the two provisions must be interpreted in harmony with each other. If there is no lawsuit condition in § 314.107(c) for a first applicant to qualify for 180-day exclusivity, FDA must disregard the lawsuit condition in § 314.94(a)(12)(viii)(B) for keeping patents listed to maintain eligibility for 180-day exclusivity after the first applicant has qualified for it under § 314.107(c).

Although it concedes that the presence of the lawsuit condition in the regulation that enforces 180-day exclusivity, and its absence from the regulation that creates 180-day exclusivity, is an "incongruity" (FTC Response at 5), the FTC argues that the lawsuit condition in § 314.94(a)(12)(viii)(B) should nevertheless continue to apply. However, the FTC's response ignores the origin of the lawsuit requirement for not delisting a patent and offers no legitimate justification for continuing it.

The origin of the lawsuit condition in § 314.94(a)(12)(viii)(B) makes clear that its sole purpose was to maintain the eligibility of first-filed paragraph IV ANDAs for 180-day exclusivity as established in § 314.107(c). Section 314.107(c) implements FDCA § 505(j)(5)(B)(iv), added by the 1984 Hatch-Waxman Amendments. FDA initially interpreted the FDCA as making 180-day exclusivity available only to first applicants that had been sued for patent infringement or had successfully defended against such a lawsuit. In Mova, the court struck down FDA's successful defense interpretation as contrary to the plain meaning of the statute. Later, in response to Mova, FDA revised § 314.107(c) to require a first applicant to meet only one condition to be eligible for 180-day exclusivity – that the ANDA contain a paragraph IV certification. IPI's ANDA for simvastatin tablets met, and continues to meet, this eligibility condition for 180-day exclusivity.

The Mova decision and FDA's revision of § 314.107(c) are explained in IPI's petition, as is the relationship between § 314.94(a)(12)(viii)(B) to § 314.107(c). (See IPI Petition at 3-7.) IPI's paragraph IV certifications to Merck's '481 and '520 patents establish IPI's eligibility for 180-day exclusivity as a legal right under the FDCA; any action by FDA that undercuts IPI's eligibility is just as unlawful as was the agency's refusal to honor Mova's eligibility. FDA's decision allowing Merck to delist the '481 and '520 patents signals that the agency will not honor IPI's eligibility for 180-day exclusivity and is therefore unlawful.

Ignoring the relationship between § 314.107(c) and § 314.94(a)(12)(viii)(B), the FTC reargues the merits of FDA's invalidated successful defense requirement. The FTC criticizes the IPI petition for saying IPI has a right to exclusivity for the simvastatin ANDA "regardless of whether the patent was the subject of successful litigation or the reasons for the delisting" (FTC Response at 5). It states that 180-day exclusivity was intended by Congress to be an incentive to "challenge weak patent claims and design products that avoid infringing narrow ones" (FTC Response at 9), and makes clear that it is referring to patents that are "successfully challenged" (FTC Response at 11), meaning that the ANDA applicant is sued and wins.

This justification for FDA's decision to delist unlitigated paragraph IV patents amounts to a repackaged version of the rejected arguments FDA pressed on the court in Mova. In addition, the FTC's justification is itself inconsistent with the FDA's policy of allowing unlitigated patents to be delisted. If 180-day exclusivity is intended as an incentive to generic drug companies to "design products that avoid infringing narrow" Orange Book-listed patents, it follows that under FDA's policy a first paragraph IV applicant that designs a noninfringing formulation will most likely be denied – not granted – the 180-day exclusivity incentive. The NDA holder commonly elects not to sue if the first applicant's paragraph IV notice demonstrates noninfringement. FDA's policy allows the NDA holder to delist the patent in that situation, therefore denying the first applicant the incentive the FTC claims it deserves.

The FTC also states that "180-day exclusivity is better viewed as an incentive, rather than a right, because neither the statute nor the regulations guarantee the first ANDA filer that it will reap the benefit of the exclusivity period" once FDA approves its generic product (FTC

Response at 9). However, the FTC's view applies equally to exclusivity based on litigated and unlitigated patents, and is therefore not relevant to the issue in the IPI petition, which relates to FDA's inconsistent treatment of generic applicants depending on which category their paragraph IV patents are in. Moreover, the FTC's view is based on false logic. A right is something that can be legally enforced if its owner has met prescribed conditions. A right does not cease to exist because its owner might be unable to take advantage of it.

Some examples the FTC gives for how a first applicant may not benefit from 180-day exclusivity are actually examples in which the applicant no longer meets the prescribed eligibility conditions. Those examples are irrelevant. The fact that the owner of a right may no longer qualify for the right due to changed circumstances does not, any more than its inability to take advantage of the right, mean there was no right to begin with. The IPI petition acknowledges that eligibility for 180-day exclusivity can be lost due to changed circumstances (IPI petition at pp. 7-8), but, as the petition points out, an NDA holder's patent delisting request is not one of those circumstances.

The FTC's examples are, in any event, inapposite to IPI's ANDA for simvastatin. The FTC points out that ANDAs that no longer contain paragraph IV certifications because the patent has expired will not be subject to the first applicant's 180-day exclusivity. However, FDA's position is that the first applicant's eligibility for 180-day exclusivity does not survive patent expiration. FDA's position is arguable either way, but it has nothing to do with IPI's eligibility for 180-day exclusivity based on paragraph IV certifications to the '481 and '520 patents, which will not expire until 2008 and 2009. After Mova, NDA holders such as Merck cannot be permitted to eliminate the underpinnings of 180-day exclusivity by delisting unexpired patents on the irrelevant ground that the first applicant was not sued for infringement.

The FTC gives the example of an NDA for which the patent "has been removed from the Orange Book," thereby precluding paragraph IV certifications and 180-day exclusivity. (FTC Response at 10.) This example begs the central question the IPI petition raises. To argue that a first-filed paragraph IV ANDA loses its eligibility for 180-day exclusivity when a patent is delisted is completely circular if the only reason the FDA allows the patent to be delisted is its

belief that the ANDA is not eligible for 180-day exclusivity to begin with. That FDA signals its conclusion about eligibility for 180-day exclusivity by allowing NDA holders to delist patents cannot insulate FDA from a challenge to the validity of the conclusion itself.

The FTC also cites the example of 180-day exclusivity triggered at a time when the first applicant cannot market its product because its ANDA is not yet approved. Id. But the first applicant can benefit from the exclusivity by, for example, selectively waiving it in exchange for consideration. The example therefore does not support the proposition for which the FTC cites it.

Even if this and the FTC's other examples stood for that proposition, however, the proposition is irrelevant. Whether IPI has a right to eligibility for 180-day exclusivity for the simvastatin ANDA, and therefore to have FDA reinstate the '481 and '520 patents, does not depend on whether IPI may lose its eligibility for reasons unrelated to FDA's unlawful delisting decision or may not be able to take full advantage of that exclusivity when its ANDA is approved in 2006. Rather, IPI's right to eligibility depends on FDCA § 505(j)(5)(B)(iv) as interpreted in Mova and implemented by FDA in § 314.107(c). Those authorities unambiguously establish that IPI is eligible for 180-day exclusivity. FDA would not argue that it may disregard IPI's right directly, by simply declaring that IPI is not eligible for exclusivity even though it has met the conditions of § 314.107(c). It follows that the agency cannot logically argue that it may do so indirectly, by allowing Merck to delist the '481 and '520 patents in reliance on language whose only purpose is to give effect to eligibility under § 314.107(c) but which contains an anachronistic reference to a previous version of § 314.107(c) that was struck down in Mova.

2. The merits of patent listings are irrelevant to 180-day exclusivity.

The FTC says it is important that a "viable mechanism for correcting erroneous Orange Book patent listings exist" and that if an NDA holder "realizes it erred in submitting patents, as Merck presumably did, [the NDA holder] should be able to correct the error" (FTC Response at 9). Earlier in its response, the FTC suggests, although it does not assert, that the '481 and '520

patents on Zocor do not qualify for Orange Book listing under FDA's regulations, because "neither patent claims simvastatin itself or its use." The FTC states that the IPI petition is wrong in "characterizing its eligibility for the 180-day exclusivity [for the simvastatin ANDA] as a right . . . which cannot be divested even when that eligibility is based on an erroneously listed patent" (FTC Response at 9).

The FTC confuses eligibility for 180-day exclusivity under FDCA § 505(j)(5)(B)(iv) with the test for patent listing in FDCA §§ 505(b)(1) and (c)(2). A first-filed paragraph IV ANDA qualifies for 180-day exclusivity under § 505(j)(5)(B)(iv) whether the patent to which the certification is made was listed correctly or incorrectly. That is FDA's position, not IPI's. Since before 1998 as to listed patents on which infringement suits were brought, and since 1998 as to listed patents not involving lawsuits, as well, FDA has consistently interpreted § 505(j)(5)(B)(iv) as making 180-day exclusivity available as long as the first applicant has submitted a paragraph IV certification to a patent, without regard to whether the listing of the patent is later believed by the NDA holder to have been incorrect.

If that were not FDA's position, the agency would have denied 180-day exclusivity to the mirtazapine and brimonidine paragraph IV ANDAs (see IPI petition at pp. 18-21). In the case of mirtazapine, at the time Organon requested to delist its patent the court hearing the paragraph IV patent infringement suits brought by Organon had already raised a substantial issue about the propriety of the patent listing, and Organon was at that time facing antitrust allegations premised in part on a wrongful listing theory. In the case of brimonidine, the court hearing the paragraph IV patent infringement suits brought by Allergan made clear that the patents at issue should not have been listed in the Orange Book to begin with. Yet in both cases FDA rejected the contention of subsequent ANDA applicants that the first applicant's ANDA should not be granted exclusivity for that reason. Indeed, in the case of mirtazapine, FDA specifically refused Organon's delisting request, not because the mirtazapine patent listing was correct but because the listing had to remain in the Orange Book to preserve the first applicant's eligibility for 180-day exclusivity. Although Organon might have been concerned at the time that the mirtazapine patent listing might be "erroneous" and sought to "correct" it, the FDA required the

listing to remain because that is how the FDCA's mechanism for giving effect to exclusivity under section 505(j)(5)(B)(iv) works.

The IPI petition is not about correct and incorrect patent listings. It is about litigated and unlitigated paragraph IV patents, and FDA's inconsistent treatment of first-filed ANDA applicants with respect to 180-day exclusivity in cases where (a) the paragraph IV patent is unlitigated and (b) the NDA holder requests delisting of the patent. FDA does not let NDA applicants delist litigated patents if doing so undercuts 180-day exclusivity. But it does so, as in the Zocor and Serzone cases, when the patents have not been litigated. This inconsistent treatment is in direct violation of 21 C.F.R. § 314.107(c) as amended after Mova.

The IPI petition explains the inconsistency and asks FDA to rectify it. The FTC's response does not address the point of the IPI petition, except to say that the "incongruity" on which FDA's policy is based is justified because ANDA applicants that successfully defend lawsuits are more deserving of 180-day exclusivity (FTC Response at 10), a factor FDA cannot lawfully rely on after Mova.

3. That the Orange Book patent listing mechanism should be improved does not relate to IPI's requested relief.

Instead of addressing IPI's basis for relief, the FTC argues for the necessity of a "viable mechanism to correct erroneous patent listings." The FTC's plea echoes what generic drug companies have been requesting for a decade, to no avail. FDA has taken the position, upheld by the courts, that there is, and can be, no mechanism for "correcting" patent listings. In FDA's system, the decision to list or delist a patent under FDCA §§ 505(b)(1) and (c)(2) is left to the unreviewable judgment of the NDA holder. If the NDA holder lists a patent that is not eligible, ANDA applicants have no choice but to certify to it. If the NDA holder fails to list, or requests delisting of, a patent that is eligible, ANDA applicants have no way to require the patent to be listed. Only if an ANDA contains a paragraph IV certification to a patent does FDA refuse to delist a patent, and it does so not because the patent qualifies under §§ 505(b)(1) and (c)(2) but because the patent must remain listed to support 180-day exclusivity under § 505(j)(5)(B)(iv).

The FTC implies that Merck, as a result of FDA's 2003 amendment to the agency's patent listing, realized that the '481 and '520 patents were no longer eligible for listing and sought to "correct" the Orange Book by requesting that they be removed. But neither IPI nor the FTC can know whether Merck believed the patents to have been, or to have become, incorrectly listed, or simply decided in September 2004 that it preferred them not to be in the Orange Book for other reasons. The timing of Merck's delisting request, seen by the FTC as evidence that Merck was correcting a mistake it realized it had made after FDA clarified the rules, hardly suggests a cause-and-effect relationship: the final FDA patent listings regulations were issued in June 2003, and Merck only requested delisting of its patents 15 months later.

Moreover, in 2000, when the '481 and '520 patents were listed, there was no consensus about the "listability" of many types of patents routinely submitted by NDA holders. Merck's patents were within the range of patent types typically listed in the Orange Book at the time of IPI's paragraph IV certifications, and therefore the FTC's suggestion that IPI is less entitled to 180-day exclusivity because the listings have been "corrected" is not only legally irrelevant but factually wrong.

But even if Merck's delisting decision was motivated by a belief that the '481 and '520 patents were erroneously listed, it is still the case that FDA provides no mechanism for "correcting" patent listings. Instead, FDA permits NDA applicants to make unilateral changes in patent listings, subject only to self-policing under the general duty not to make false statements to the government. The FTC's characterization of NDA holders' patent delisting requests as a "viable mechanism for correcting erroneous Orange Book patent listings" is accurate only if it is assumed that NDA holders have not only the legal responsibility under the FDCA to list patents but also the legal authority to validate their own judgments about whether patents are eligible for listing, remain eligible, or are ineligible and should be delisted. Not even FDA goes so far as to characterize such NDA holders' judgments as "correct" under the FDCA. It simply declines to second-guess them.

If, for argument's sake, delisting of the '481 and '520 patents constituted a "correction," Merck's decision to list the '481 and '520 patents in 2000 nonetheless required IPI to certify to

those patents. By certifying, IPI qualified for 180-day exclusivity as a matter of legal entitlement under the FDCA as interpreted in Mova and applied by FDA in § 314.107(c) as amended after Mova. IPI's right cannot be extinguished by Merck's decision to delist the patents, whether or not Merck should have listed them to begin with or came to believe they no longer met the listing standards in FDA's regulations.

4. Orange Book abuse is caused by lawsuits not listings.

Putting aside that it cannot be known whether an NDA holder's delisting is a "correction," the FTC's response to the IPI petition takes aim at the wrong target. The FTC response (at 7-9) describes at length the specific anticompetitive arrangements the agency has acted against and the pattern of generic drug market entry delays it has studied, all supposedly attributable in some way to patent listing under the Hatch-Waxman provisions of the FDCA. But patent listing is only a short-hand reference to the real cause of delayed generic drug market entry – the patent infringement lawsuits NDA holders file to obtain automatic 30-month stays of ANDA approval.

In many cases, NDA holders have obtained overlapping 30-month stays based on sequentially issued patents, sometimes in conjunction with other types of Hatch-Waxman market protection. Often, the patents supporting this strategy have raised no Orange Book "listability" issues. However, some patents of questionable relevance to the approved NDA drug have appeared in the Orange Book. The FDA's 2003 regulations, and the Medicare Modernization Act of 2003 (MMA) have addressed the 30-month stay issue without regard to patent listability, and the FTC has pursued sanctions against NDA holders who used questionable patent listings to obtain 30-month stays.

The 30-month stay is not a factor, however, when the NDA holder does not sue the first ANDA applicant for infringement of a listed patent. Indeed, the FTC found that there is generally no interference with generic drug market entry when no lawsuit is brought in response to a paragraph IV certification:

> The data show that when the brand-name company did not sue the first generic applicant for patent infringement (29 drug products, see Table 2-1), the first generic applicant began commercial marketing soon after receiving FDA approval.

Study at 58. Thus, even if a patent is erroneously listed, and a generic applicant submits a paragraph IV certification, in the absence of a patent infringement lawsuit, the listing itself does not result in delayed approval or marketing. In comparison, as the FTC study found, infringement lawsuits typically produce substantial delays. See Study at 39-56. Similarly, the FTC enforcement actions referred to in the FTC's response to the IPI petition all involved conduct based on litigated patents, not patents on which no infringement lawsuits were brought.

In light of the foregoing, the FTC's view that delays in generic drug market entry are addressed by FDA's policy of allowing NDA holders to delist nonlitigated patents is unfathomable. The FTC states:

> Delays in generic entry produced by the inability to delist patents from the Orange Book are contrary to that policy. Therefore, it is important that a viable mechanism for correcting erroneous Orange Book patent listings exist. An NDA holder that realizes it erred in submitting patents for listing, as Merck presumably did, should be able to correct that error. To avoid consumer harm, an NDA holder seeking to delist a patent in compliance with an FTC or court order must also be allowed to do so.

FTC Response at 9.

The quoted statement begins with the false premise that delays in generic drug approvals are caused by Orange Book patent listings, and the inability of NDA holders to delist patents. They are not. Delays in generic drug approvals are caused by NDA holders bringing infringement lawsuits on the patents they have listed. If there is no infringement lawsuit, there is no delay.

An NDA holder is not required to sue for infringement just because it has listed a patent in the Orange Book. Nor does the presence of a patent listing in the Orange Book, even an incorrect patent listing, generate some mysterious force that overpowers the NDA holder's desire not to delay generic competition and compels it to file an infringement lawsuit it would rather

not bring. NDA holders are fully capable of not delaying ANDA approvals by deciding, of their own free will, not to sue on patents that are, and that remain, listed in the Orange Book, erroneously or otherwise. They are also capable of making the opposite decision.

For this reason, the "viable mechanism for correcting erroneous Orange Book patent listings" the FTC insists is necessary to "avoid consumer harm" from "delays in generic drug entry" is completely irrelevant. Patent listings don't delay generic drug entry. Patent infringement lawsuits delay generic drug entry. An NDA holder can leave an erroneous patent listing in the Orange Book indefinitely and cause no delay in generic approval as long as it does not sue. On the other hand, an NDA holder that intends to delay generic drug approval by filing an infringement lawsuit is not going to be prevented from doing so by the existence of a "viable mechanism" that allows it to voluntarily delist the patent on which its lawsuit will be based.

Even if the FTC's "viable mechanism" was a solution to the problem of delay in ANDA approvals, the FTC's support for the FDA policy challenged in the IPI petition is paradoxical. The FDA policy prohibits the delisting of an erroneously listed patent when the NDA holder has actually used it to delay generic approval by filing an infringement lawsuit. The only paragraph IV patents the FDA policy allows NDA holders to delist are the ones that do not cause delays, because the NDA holders have decided not to sue for infringement.

The FTC's response contains a useful illustration of the failure to grasp the essential fact that the FDA's policy is contradictory of the FTC's reasons for supporting it. The FTC contends that allowing NDA holders to delist patents will allow them to make corrections that, in turn, will reduce delays in generic market entry. As an example, the FTC notes that it dropped its investigation of GlaxoSmithKline (GSK) over Paxil after GSK "voluntarily delisted three patents from the Orange Book, removing the 30-month stay on generic approval" (FTC Response at 7). In actuality, despite GSK's request, FDA refused to remove the '759 and '233 patents from the Orange Book, allowing GSK to delist only the '927 patent. FDA said "TorPharm is eligible for 180-day exclusivity as to the '759 and '233 patents. Therefore, FDA will not remove those patents from the Orange Book until the 180-day exclusivity period has expired." Letter, G. Buehler to Apotex Corp., July 30, 2003.

If the FTC's reason for supporting the FDA's policy were valid, the FDA would have delisted the '759 and '233 patents, because they were the ones causing delays, in the form of 30-month stays, in generic drug competition for Paxil. But because the '759 and '233 patents were litigated, and therefore supported 180-day exclusivity, FDA refused to delist them. FDA's refusal, however, did not prolong the delay in generic drug entry, because FDA stepped around the 30-month stay by concluding that "GSK has effectively abandoned its claim to" it.

The GSK example contradicts the FTC's support for FDA's policy as necessary to avoid delays in generic drug entry in three ways:

- FDA's policy does not allow NDA holders to delist patents that are delaying generic drug entry.
- The patents NDA holders are allowed to delist are not the ones delaying generic drug entry.
- FDA does not need to offer a "viable mechanism" for patent delisting to avoid delays in generic drug entry from patents that remain listed in the Orange Book.

5. Parking problems occur when patents are litigated.

The FTC claims that, "[w]ere FDA's regulations to prohibit delisting as IVAX argues, there would be no means by which to stop the on-going consumer harm caused by a 'parked' 180-day exclusivity period." (FTC Response at 8.)

FDA's regulations already prohibit delisting patents associated with "parked" 180-day exclusivity, i.e., patents on which infringement lawsuits are brought, as described by the FTC. However, the FTC ignores the fact that such agreements are often reached after protracted litigation and therefore do not account for market conditions or the risks of litigation. In certain situations, an agreement to "park exclusivity," for a period of time but less than the period remaining on the patent life, may be a realistic option when an NDA holder has sued the first

ANDA applicant for infringement. Within the framework of a patent infringement dispute litigated in court, an agreement involving 180-day exclusivity may well be valid as part of settling the lawsuit in good faith, even if it is subsequently criticized by the FTC or the courts. Therefore, to the extent that Orange Book patent listings by themselves (as opposed to the lawsuits voluntarily filed by NDA holders) contribute to exclusivity parking arrangements, granting IPI's petition would have no effect on the "on-going consumer harm" the FTC says they cause.

IPI's petition asks only that, in addition to patents that are the subject of infringement lawsuits, FDA also prohibit the delisting of those that are not. Patents that are not the subject of infringement lawsuits are not associated with exclusivity parking problems. Without a patent infringement lawsuit, an agreement between an NDA holder and an ANDA applicant to park 180-day exclusivity would have little justification and therefore would be unlikely to emerge as a plausible subject for consideration by an NDA holder and a first ANDA applicant. The FTC response provides no evidence that questionable agreements involving 180-day exclusivity have been the source of delayed generic drug market entry when the exclusivity has been based on unlitigated patents.

6. FDA's policy invites abuse.

The FTC's response to IPI's petition defends FDA's policy because it allows NDA holders to "correct" erroneous patent listings. According to the FTC, the ability to correct patent listings addresses the problem of abuse of the Hatch-Waxman system consisting of listing questionable patents in the Orange Book and forcing ANDA applicants to certify to them.

But, as shown in section 3, FDA's policy only allows NDA holders to remove patent listings. Whether the removal involves a "correction" cannot be determined by any existing administrative procedure in FDA's Hatch-Waxman system. As shown in section 4, abuse of the Hatch-Waxman system may involve listing questionable patents, but only as part of NDA holders' larger strategy of filing infringement actions. Offering NDA holders an opportunity to voluntarily delist questionable patents, which is all FDA's policy provides for, does nothing to

deter use of that larger strategy. Finally, FDA's policy does not allow NDA holders to voluntarily delist patents that are, in fact, used to delay generic drug entry by supporting paragraph IV infringement actions and 30-month stays. It only allows them to delist patents they have decided not to use to delay generic drug entry.

As irrelevant as it is to any of the advantages the FTC attributes to it, FDA's policy does have a relevant effect that is contrary to the FTC's goal of reducing anticompetitive abuses of the Hatch-Waxman system. That effect consists of giving NDA holders the ability to destroy the value of the 180-day exclusivity incentive for generic drug companies to develop competing products.

The value of an economic benefit as an incentive depends on the certainty of its availability to the company that engages in the conduct the incentive is meant to bring about. The 180-day exclusivity incentive is meant to encourage generic drug companies to develop generic versions of patented brand name drugs, and to do so quickly. A generic company that is first to file an ANDA with a paragraph IV certification qualifies for the benefit of 180-day exclusivity, and therefore generic drug companies have a strong incentive to accelerate the development of widely prescribed brand name drugs.

Under § 314.107(c), the first applicant fulfills all statutory eligibility requirements for 180-day exclusivity immediately upon acceptance of its substantially complete ANDA with a paragraph IV certification. Of course, to benefit from the exclusivity, the applicant must obtain approval of the ANDA. Under the MMA, it must also market the drug within 75 days of a forfeiture event. There are other circumstances in which, pursuant to statute or FDA's interpretation of it, the first applicant may lose eligibility for, or be unable to benefit from, 180-day exclusivity. With these several limits, 180-day exclusivity is a strong incentive for generic companies to be first to file, thereby accelerating generic drug market entry.

FDA's policy weakens the 180-day exclusivity incentive by subjecting its availability to the decision of an NDA holder to withdraw the patent on which the first applicant's paragraph IV certification is based. This is a decision over which the ANDA applicant has no control, and it is

an eventuality it has no ability to predict. From the NDA holder's side, delisting costs nothing, because the NDA holder has already decided it will not sue for infringement (if it has not, it won't delist the patent, and if it sues, FDA won't let it), and therefore withdrawing the patent has no additional effect relating to its rights under the Hatch-Waxman provisions of the FDCA

But delisting the patent does adversely affect the NDA holder's future generic competitor. By making a cost-free, one-page, unexplained delisting request to FDA, the NDA holder can reduce the value of the first applicant's ANDA to nothing, costing the generic company tens of millions of dollars. This life-or-death power over a first applicant's exclusivity gives the NDA holder substantial economic leverage. Whether NDA holders will take advantage of this leverage, either to pursue specific anticompetitive objectives, or simply to reduce the overall business incentive for generic drug development, is of course impossible to say. But it would be well for the FTC, with its lengthy history of having to police the territory governed by the Hatch-Waxman provisions of the FDCA, to keep in mind the reality that businesses seek competitive advantages as surely as water seeks its own level.

7. The MMA.

We agree with the FTC (FTC Response at 3, 9) that the issues raised by the IPI petition are likely to be relevant under the MMA. The changes made by the MMA do not affect eligibility for 180-day exclusivity. To be eligible under either version of the exclusivity provision, an ANDA applicant must file an ANDA with a paragraph IV certification before another such ANDA is filed, and under either version there is no requirement that the applicant be sued for patent infringement. Compare FDCA § 505(j)(5)(B)(iv)(II)(bb) (MMA) with § 505(j)(5)(B)(iv) (pre-MMA). The mechanics of providing 180-day exclusivity also remain the same: FDA cannot approve a subsequent ANDA for 180 days if, like the previous ANDA, it contains a paragraph IV certification. Compare FDCA § 505(j)(5)(B)(iv)(I) (MMA) and § 505(j)(5)(B)(iv) (pre-MMA).

Under FDA's regulations, for the previous and subsequent ANDAs to be considered as "containing" a paragraph IV certification, the patent to which the certification applies must be

listed in the Orange Book. It follows that, to give effect to 180-day exclusivity, FDA must, under the MMA as under the original law, require patents on which paragraph IV certifications are based to remain in the Orange Book even if the NDA holder asks that they be delisted. Because the MMA, like the 1984 provisions, does not condition eligibility for 180-day exclusivity on a patent infringement lawsuit, FDA must require a patent to remain in the Orange Book even if the first applicant (or any other applicant) is not sued for infringement, notwithstanding an NDA holder's request to delist the patent.

Unlike the 1984 statute, the MMA contains provisions under which 180-day exclusivity is forfeited. The FTC cites one of those provisions as supporting its argument that, even if an ANDA applicant meets all legally applicable eligibility conditions, "removing improperly and erroneously listed patents from the Orange Book" causes them to lose 180-day exclusivity: "[t]he MMA goes farther [in allowing changed circumstances to affect 180-day exclusivity] by allowing ANDA applicants to challenge patent listings in a counterclaim and by listing withdrawal of a patent from the Orange Book as a forfeiture event for . . . 180-day exclusivity" (FTC Response at 11).

The FTC is referring to the provision added by the MMA that allows first ANDA applicants sued for patent infringement to counterclaim for an order requiring the NDA holder to correct or delete patent information. FDCA § 505(j)(5)(C)(ii)(I). Withdrawal of the patent from the Orange Book pursuant to such an order creates a failure to market forfeiture event. FDCA § 505(j)(5)(D)(i)(I)(bb)(CC). But the FTC is wrong that this forfeiture provision recognizes withdrawal of a patent as one of the "changed circumstances" that cause eligibility for 180-day exclusivity to be lost. It does the opposite. It explicitly acknowledges that the first applicant's eligibility for 180-day exclusivity continues for 75 days after the patent has been removed and then, if the first applicant markets the drug before the forfeiture period expires, for an additional 180 days, i.e., the exclusivity period itself. The FTC's example simply reinforces the point made in the IPI petition: once it is established, eligibility for 180-day exclusivity cannot be negated by Orange Book mechanics.

The prohibition against delisting patents in § 314.94(a)(12)(viii) is part of the mechanics for enforcing 180-day exclusivity for which eligibility is established under § 314.107(c). Section 314.94(a)(12)(viii) refers to patents that are the "subject of a lawsuit" because, when it was written, the eligibility conditions for 180-day exclusivity included being sued for patent infringement. After Mova, the eligibility conditions were revised. They no longer include being sued for infringement. FDA may not lawfully apply a pre-Mova mechanism for enforcing 180-day exclusivity to deny exclusivity to a first applicant that met, and continues to meet, post-Mova eligibility conditions.

Conclusion

For the reasons above and in IPI's January 5, 2005, citizen petition and April 11, 2005, supplement to the citizen petition, the actions requested in the citizen petition should be taken.

Respectfully submitted,

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