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BY HAND DELIVERY

December 23, 2002

Dockets Management Branch
Food and Drug Administration
5630 Fishers Lane
Room 1061 - HFA-305
Rockville, Maryland 20852

Re: Docket No. 02N-0417
Comments on Proposed Rule Amending Patent Listing Requirements for New Drug Applications and Applicability of 30-Month Stays on Approval of Abbreviated New Drug Applications

Dear Madam/Sir:

We represent Organon Inc., 375 Mt. Pleasant Avenue, West Orange, New Jersey 02052 (“Organon”). On behalf of Organon, we herewith submit the following comments to the Food and Drug Administration (FDA) in response to the Agency’s Proposed Rule, published in the Federal Register on October 24, 2002, to amend its regulations implementing the Drug Price Competition and Patent Term Restoration Act (the “Hatch-Waxman Act” or “the Act”). 67 Fed. Reg. 65448 (Oct. 24, 2002).

In these comments, Organon addresses the following proposed changes in Agency policy:

- (1) FDA’s proposal to limit the listing of use patents in the Orange Book to only those that claim an approved use; and
- (2) FDA’s proposal to provide for only a single 30-month stay of approval of an Abbreviated New Drug Application (ANDA) containing a certification that a patent claiming a drug is invalid or will not be infringed.

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I. FDA's Proposal to Limit Listing of Use Patents to Those Claiming an Approved Use

A. The Proposal contradicts the plain language of the Hatch-Waxman Act.

The FDA's proposal to bar the listing in the Orange Book of any use patents other than those that claim an approved use of the listed drug runs contrary to the plain language of the Hatch-Waxman Act. The Act specifically requires a submitter of an NDA to list in the Orange Book "any patent which claims 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). 21 U.S.C. § 355(b)(1). Notably absent from this provision is any language whatsoever limiting the requirement to patents that claim an approved use of the drug. Nor do the relevant provisions of the Patent Act impose any such restriction on patent listing.¹

The statute indicates that applicants must file patent information about "any patent which claims the drug for which the applicant submitted the application, or which claims a method of using such drug. . . ." 21 U.S.C. § 355(c)(2). Clearly the statute does not say "any patent which claims an approved method of using such a drug," even though this is the interpretation now advanced by the FDA. Thus, the Agency, in this Proposal, is now seeking to change the plain meaning of the statute.

¹ The relevant provisions of the Patent Act, as amended by Hatch-Waxman, are codified at 35 U.S.C. § 271(e).

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The phrase on which the FDA's erroneous interpretation hinges is this: "for which the applicant submitted the application." To sustain its interpretation, the Agency must intend to read that phrase to modify another phrase, namely, "method of using such drug." But the former does not modify the latter. Instead, the phrase "for which the applicant submitted the application" modifies the phrase "the drug." In other words, the statutory requirements pertain to "*the drug* for which the applicant submitted the application." Nothing in the plain language of the statute suggests that the key phrase should be read so as to modify another phrase, "method of using such drug." Accordingly, the statute, as written and enacted by Congress, does not support the Agency's proposal to limit the listing of use patents to only those claiming an approved use. Rather, under the statute's clear language, provided that a drug is the subject of a pending or approved NDA, the NDA applicant must submit for listing in the Orange Book any patent that claims a method of using "such drug" and for which a claim of patent infringement may reasonably be asserted. This is so regardless of whether that method of use itself is the subject of a pending or approved NDA. 21 U.S.C. § 355(b)(1).

The Agency's proposal to limit use patents eligible for Orange Book listing to only those patents that claim an approved use also conflicts with the relevant provision of the Patent Act, which states that it is an act of infringement to submit an ANDA "for a drug claimed in a patent or the use of which is claimed in a patent." 35 U.S.C. § 271(e)(2). In a manner analogous to and fully consistent with the patent listing requirement, nowhere does the Patent Act limit an infringement action to only those use patents that claim an *approved* use.

B. The Proposal undermines the legislative goals of the Hatch-Waxman Act.

Not only does FDA's restriction on use patents conflict with the plain language of the Hatch-Waxman Act, it also upsets the delicate balance – carefully crafted by Congress – between drug innovation and the availability of generics. In drafting the Hatch-Waxman Act, Congress carefully crafted the statutory language so as to strike a balance between two competing policy interests: (1) encouraging the research and development of innovator drugs and new therapies; and (2) enabling competitors to bring low-cost generic copies of those drugs to market.

The legislative history demonstrates that as Congress sought to reduce the time and expense to gain approval for a generic drug, it took great pains to protect the substantial investment made by innovator companies by according them full patent rights in new drugs and uses for those drugs. See H.R. REP NO. 857, 98th Cong., 2d Sess., pt. 1, at 14-15, reprinted in 1984 U.S. CODE CONG. & ADMIN. NEWS 2647, 2647-48. Yet these protections – protections offered by Congress in exchange for policies greatly benefiting the generic-drug industry – are significantly undermined by the FDA's Proposed Rule. By broadly referring to the listing of patents covering uses of an approved drug, and broadly permitting filing of a patent infringement action based on patents covering uses of an approved drug, Congress implemented its stated objective of encouraging research and development of new therapies for both old and new drugs.

Such a restriction also conflicts with another important goal of the Hatch-Waxman Act: to resolve questions of infringement prior to a generic's market entry. To accomplish this objective, the Act recognizes a new form of patent infringement, the Paragraph IV certification. The proclaimed purpose of this cause of action was to expedite the process of resolving competing

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intellectual property claims and thereby to protect name-brand innovators' rights and to prevent generic companies from expending the considerable time and capital required for ANDA approval on a generic product that is subsequently found to be infringing. Yet this critical objective is thwarted by FDA's proposal to restrict the type of use patents that are eligible for protection under the Act.

The problem arises as a consequence of the following. Under the Agency's new interpretation of the Hatch-Waxman Acts, NDA holders would not be permitted to list in the Orange Book certain of their valid use patents. Consequently, ANDA applicants would not file a Paragraph IV certification regarding those patents, because there can be no Paragraph IV certification in the absence of an Orange Book listing. Yet, listed or not, the patent is valid and therefore can form the basis of a patent infringement suit. The effect of the regulation is to deny the potential for pre-market resolution of the validity of the patent, forcing the generic company to choose between coming to market and facing massive damage claims or choosing not to proceed. This is precisely the dilemma that Congress sought to avoid in enacting the Hatch-Waxman Act.

FDA's overly restrictive interpretation not only undermines the intent of the Act to resolve patent disputes early, it is also evidence of the Agency's misunderstanding of patent law. Specifically, FDA appears to believe that patent infringement arises only when a party submits an ANDA for a (patented) use *claimed in an NDA*. But this is simply not the case, for patent infringement does not depend on whether the use is claimed in an NDA. Instead, the proper inquiry is simply "whether, if a particular drug were put on the market, it would infringe the

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relevant patent.” *Bristol-Myers Squibb Co. v. Royce Labs, Inc.*, 69 F.3d 1130, 1135 (Fed. Cir. 1995).

A brief review illustrates one way that patent infringement could arise for a situation other than marketing a drug for an approved use. First, a patent that claims a use not specifically set forth in the FDA-approved labeling is nonetheless valid; its legitimacy as a patent depends entirely upon particular technical specifications, not on the FDA approval process. Where a generic copy of that drug is prescribed for such a patented, non-labeled use, the use patent is infringed. It is a common practice of physicians to prescribe a drug for such indications or uses. Moreover, it is also common practice of physicians and pharmacists to substitute a generic drug for an innovator drug. Thus, infringement of patents for off-label uses is hardly speculative but, instead, entirely predictable. Where the NDA holder has exclusive patent rights in a particular use of a drug – whether approved or off-label – it may “reasonably assert” those rights in connection with the marketing of a generic copy of that drug that likely will be prescribed for such use.

In addition to the serious problems outlined above, there is yet another reason that FDA’s proposed change cannot withstand scrutiny: the interpretation fails to account for the actual complexities of patents and approved uses. Since FDA is neither charged with, nor expert in, the assessment and adjudication of patent claims, this policy error is not surprising. It is easy to believe mistakenly that patents and their claims can be parsed into specific categories such as composition, formulation, and method of use patents. Yet such matters are typically quite complex.

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At a minimum, therefore, where a patent claims a use, the applicant should be permitted to list it in the Orange Book, provided the use pertains to the drug that is the subject of the NDA.

Whether such a patent is in fact valid and infringed is a matter to be determined through litigation initiated by a Paragraph IV certification, not through the overly simplistic test proffered by the Agency.

II. FDA's Proposal to Limit Patent Holders to a Single 30-Month Stay

A. The proposed new interpretation is contradicted by the plain language of the Hatch-Waxman Act.

The 30-month stay provision is one of the most important intellectual property protections that the Hatch-Waxman Act offers innovator companies, and is key to preventing expenditure of Agency resources on approving a generic drug that is subsequently found to be infringing and therefore not marketable. Under the Hatch-Waxman Act, a 30-month stay is triggered where an ANDA applicant certifies, under Paragraph IV, that the patent is invalid or not infringed, and where patent infringement litigation ensues. 21 U.S.C. § 355(j)(2)(A)(vii), 21 U.S.C. § 355(c)(3)(C). Approval of the ANDA is stayed for 30 months while the litigation is pending, subject to modification by the court. 21 U.S.C. § 355(j)(5)(B)(iii), 21 U.S.C. 355(c)(3)(C).

As FDA itself acknowledges, the Agency has consistently maintained over the years that the Hatch-Waxman Act permits multiple 30-month stays of an ANDA approval. 67 Fed. Reg. 65448, 65454 (Oct. 24, 2002). However, FDA now seeks to reverse this longstanding interpretation. Instead, the Agency proposes to limit ANDAs to a single 30-month stay. Under this new proposal, ANDA applicants would still be required to make a Paragraph IV certification

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where applicable, but any subsequent Paragraph IV certifications to that same ANDA would not be subject to a 30-month stay. This proposal runs counter to the plain language of the Hatch-Waxman Act and to the intent of Congress, as evident in the Act's legislative history.

FDA attempts to justify its proposed revised interpretation as follows: Section 505(j)(2)(B)(iii) of the Hatch-Waxman Act states that whenever an ANDA is amended to "include" a Paragraph IV certification, the ANDA applicant must give the NDA holder and the patent owner notice of such certification. As justification for its proposed single 30-month stay, the Agency asserts that if the ANDA already included a Paragraph IV certification, then subsequent amendments to ANDAs -- even those that include another Paragraph IV certification -- do not trigger the notice requirement because they cannot have been made to "include" a Paragraph IV certification. Consequently, the FDA further asserts, under section 505(j)(5)(B)(iii) of the Act, only one 30-month stay per ANDA is possible because the subsequent Paragraph IV certifications do not result in a second notice to the patent owner and NDA holder, and the 45-day period for filing a patent infringement suit is never tolled. Since these are the statutory prerequisites for a 30-month stay, the Agency posits that subsequent stays are not available. Such an interpretation is markedly at odds with the text and intent of the statute, which manifestly treats ANDA amendments containing a Paragraph IV certification as giving rise to the same opportunity for a stay as a Paragraph IV certification contained in original ANDAs.

The process articulated by Section 355(j)(2)(B) contains three separate parts. Essentially, part (i) requires the ANDA applicant to provide notice of its Paragraph IV certification; part (ii)

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governs the content of that notice; and part (iii) governs the timing of the notice. Each of these parts is described in greater detail below.

First, Section 355(j)(2)(B)(i) requires, with a Paragraph IV certification, that the applicant agree to provide the patent owner and the NDA holder with the notice required under clause (ii) of the Section. More precisely, clause (i) states that the applicant “shall include in the application a statement that the applicant will give the notice required by clause (ii) to [the patent owner and NDA holder].”

Second, defining the required notice, clause (ii) states the following:

- (ii) The notice referred to in clause (i) shall state that an application, which contains data from bioavailability or bioequivalence studies, has been submitted . . . to obtain approval . . . before the expiration of the patent referred to in the certification. Such notice shall include a detailed statement of the factual and legal basis of the applicant’s opinion that the patent is not valid or will not be infringed.

21 U.S.C. § 355(j)(2)(B)(ii). In other words, clause (ii) identifies the specific content of the notice required in clause (i).

Third, in the case of an amended ANDA, clause (iii) identifies the timing for giving the notice described in clause (ii). Notably, of course, that notice is the one required in clause (i), which clearly applies equally to clause (iii). Clause (iii) states that “If an application is amended to include a [Paragraph IV certification], the notice required by clause (ii) shall be given when the amended application is submitted.” 21 U.S.C. § 355(j)(2)(B)(iii). In other words, clause (iii) speaks to no issue other than the timing for providing the required notice of a Paragraph IV certification that accompanies an amended ANDA.

According to the Agency's new interpretation, the phrase "to include" in clause (ii) would mean that only Paragraph IV certifications in original ANDAs can trigger the 30-month stay, and not Paragraph IV certifications in amended ANDAs; that is, FDA contends that a subsequent Paragraph IV certification does not trigger the notice requirement in clause (ii) because the ANDA is not amended solely to include a Paragraph IV certification. This argument does not bear scrutiny.

The crucial flaw in FDA's reasoning is its erasure of clause (i). In truth, clause (i) pertains to *any and all* ANDAs that include Paragraph IV certifications. That clause requires *any and all* such ANDA applicants to provide notice to the patent owner and NDA holder. Nothing in the language limits the effects of clause (i) only to original ANDAs, nor does any part of clause (iii) suggest such a limitation on the meaning of clause (i). Rather, clause (iii) speaks only to the timing at which the notice must be given – an important clarification given that questions of timing will inevitably arise with amended ANDAs. This provision in no way limits the notice requirement or the procedural rights of the NDA holder and/or patent owner that result from receiving that notice.

FDA's proposal to limit 30-month stays to a single one is also flatly contradicted by the following statement in the legislative history: "In the case where the patent certification is amended in an ANDA to allege invalidity or non-infringement of a patent, the FDA may not make the approval effective within the 45-day period that an action for patent infringement may be brought." H.R. Rep. No. 857, 98th Cong., 2d Sess., part 1, at 28 (1984). The 45-day provision is part and parcel of the same provision dealing with the 30-month stay. There is no way that the 45-

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day provision could apply without the 30-month stay being triggered by infringement litigation brought during the 45-day period. So when Congress made clear that the 45-day period applies to amended ANDAs with Paragraph IV certifications, it became equally clear that the 30-month stay applies as well.

Moreover, FDA's proposal to limit ANDAs to a single 30-month stay has severe, unintended consequences. For example, under this approach, ANDA applicants could circumvent *any and all* 30-month stays simply by filing twice. The process would work as follows: First, the applicant would file a flawed, original ANDA that "erroneously" contains a Paragraph III certification or, possibly, no certification whatever. When the Agency refused to accept the application, the applicant would file an "amended" ANDA, which would include a Paragraph IV certification. Although these "amendments" would be intended to cure the facial deficiency that caused the original denial, 21 C.F.R. § 314.10(b)(3)(ii), they would in fact represent an end-run around the Hatch-Waxman Act's protections of valuable intellectual property.

B. The FDA's Reversal of its prior longstanding interpretation is owed no deference.

In FDA's Federal Register Notice announcing the Proposed Rule, the Agency concedes that it has "consistently maintained that the Hatch-Waxman Act creates the opportunity for multiple 30-month stays to an ANDA's approval date" in the context of a Paragraph IV certification and responsive patent infringement action brought within the 45-day period. 67 Fed. Reg. 65448, 65454 (2002). For the following reasons the proposed revised interpretation permitting only a single 30-month stay should be rejected as invalid, and the Agency should

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maintain its longstanding practice of staying its approval of an ANDA for up to 30 months whenever an ANDA, or amended ANDA, containing a Paragraph IV certification is filed.

First, as discussed in Section II.A. *supra*, Congress directly spoke to the precise matter in question and it spoke clearly. The FDA's creative efforts to maneuver an alternative interpretation fail, because the clear and plain language of the statute as to this point leaves no room for interpretation. If the intent of Congress is clear, then the courts and the agency must give effect to the unambiguously expressed intent of Congress. *Chevron, U.S.A., Inc. v. Natural Resources Defense Council, Inc.*, 467 U.S. 837, 842-843 (1984).

Even were the statute not clear, however, the proposal would have to be rejected on other grounds. There are strong reasons for deferring to established policy in this matter and, in this context, FDA arguments for change fall fatally short. The deference due a statutory construction by an agency "depends crucially upon whether it was promulgated contemporaneously with enactment of the statute and has been adhered to consistently over time." *Barnett v. Weinberger*, 818 F.2d 953, 960-961 (D.D.C. 1982) (broader reinterpretation of a statutory exclusion from CHAMPUS benefits rejected). *Peters v. U.S.*, 853 F.2d 692, 700 (9th Cir. 1988) (Immigration and Naturalization Service's issuance of John Doe summonses in "abrupt change from longstanding practice" rejected); *INS v. Cardoza-Fonseca*, 480 U.S. 421, 457, fn 30 (1987) (Immigration and Naturalization Service's revised standard for withholding deportation rejected).

Deference is due to a statutory construction consistently respected since enactment, in part because "an agency's interpretation of a statute may be confirmed or ratified by subsequent congressional failure to change that interpretation." *Motor Vehicle Mfrs Assn v. State Farm*

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Mutual Auto Ins Co, 463 US 29, 32 (1983) (Department of Transportation's reinterpretation of motor vehicle safety standards rejected); *Bob Jones Univ. v. U.S.*, 461 U.S. 574, 599-602 (1983) (denial of tax-exempt status to private schools with discriminatory admissions policies affirmed because of clear violation of federal policy); *Haig v. Agee*, 453 U.S. 280, 291-300 (1981) (State Department's consistent administrative construction of Passport statute must be respected unless there are compelling indications that it is wrong). The FDA contends that its statutory reinterpretation limiting innovators to single 30-month stays is consistent with the legislative history that accompanied the passage of the Hatch-Waxman Act. 67 Fed. Reg. 65448, 65456 (Oct. 24, 2002). But the fact that Congress never voted to reassert such an interpretation over the years that more than one 30-month stay has been permitted, sharply undercuts the value of the Agency's contention.

Moreover, the Supreme Court has recognized that, "[i]n addition to consistency, courts also have considered the length of time over which an agency has adhered to its position." *Barnett v. Weinberger*, *supra* at 960; *Watt v. Alaska*, 451 U.S. 259, 273 (1981) (Department of the Interior's reinterpretation of a mineral rights distribution plan rejected). *Barnett* granted deference to an interpretation in place for 11 years, and *Watt* granted deference to one in place for 10 years. The policy of permitting more than one 30-month stay, which the FDA now seeks to repeal, has, in fact, been in place far longer: for at least the nearly two decades since the passage of the Hatch-Waxman Act in 1984.² Because of its longevity it should be accorded all the more deference.

²Although the FDA did not promulgate its final regulations implementing the patent listing provisions of Hatch-Waxman until 1994, it adopted its practice of permitting subsequent 30-month stays, where applicable, from the outset.

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The Agency's stated reasons for the intended policy change fail to meet the standard required to support revision. An agency's justifications for policy revision fail if, among other things, "the agency has relied on factors which Congress has not intended it to consider, [or] entirely failed to consider an important aspect of the problem. . ." *Motor Vehicle Mfrs Assn, supra* at 29. *SEC v. Chenery Corp.*, 332 U.S. 194, 196-197 (1947) (agency's action was based upon substantial evidence and was consistent with the authority granted by Congress). In making its case for changing policy, the FDA cites concerns such as the purported rising number of 30-month stays apparently being claimed over time and potential abuses of the Orange Book listings. But FDA never actually lays out the needed foundation for these arguments as issues that Congress intended it to consider in making policy.

More importantly, however, the Agency has failed to address important aspects of the problem at hand. The Supreme Court has acknowledged that an important consideration in policy revision is "legitimate reliance on prior interpretation." *Smiley v. Citibank S.D., N.A.*, 517 U.S. 735, 746, 116 S. Ct. 1730 (1996) (credit card late fees may be construed validly as interest under National Bank Act); *Paragon Health Network Inc v. Thompson*, 251 F. 3d. 1141, 1147, 2001 U.S. App. LEXIS 11695 (2001) (health care provider determined ineligible for exemption from Medicare routine cost limit). The tremendous long-term and risk-fraught investments already made by the innovator drug companies in legitimate reliance on the established 30-month stay policy are endangered by the proposed change. This threat of enormous harm to innovator drug makers, and its implications for their beneficiaries among the sick, must be addressed by the FDA. The neglect of these crucial concerns would surely be fatal to the agency's argument for policy,

even assuming *arguendo* that the original statute was sufficiently ambiguous to permit such reinterpretation.

With regard to its efforts to justify its reinterpretation, the agency should be reminded of the reasoning of the U.S. District Court for the District of Columbia in rejecting another of the Agency's recently proposed rules. Specifically, Judge Kennedy explained that while FDA's Proposed Rule "may well be a better policy tool than the one enacted by Congress; [and] it might reflect the most thoughtful, reasoned, balanced solution to a vexing public health problem," the issue is "not the Rule's wisdom" but rather the statutory authority of that Proposed Rule, which the court determined was lacking. *Assoc. of American Physicians and Surgeons, Inc. v. FDA*, 2002 U.S. Dist. LEXIS 19689 (D.D.C. Oct. 17, 2002).

FDA should, therefore, delete its proposal to limit 30-month stays to one per ANDA, and should instead maintain its longstanding position that the Hatch-Waxman Act requires a stay of up to 30 months on the Agency's approval of an NDA whenever a Paragraph IV certification is made, regardless of whether that certification is part of an original or an amended ANDA.

III. Conclusion

For the foregoing reasons, FDA should either withdraw its Proposed Rule or, at a minimum: (1) clarify that certain use patents are eligible for listing without regard to whether they



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claim an explicitly approved use; and (2) continue its longstanding policy of imposing up to a 30-month stay on the approval of an ANDA whenever the ANDA, or an amendment to that ANDA, contains a Paragraph IV certification.

Respectfully submitted,

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