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# Client Alert

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## INTELLECTUAL PROPERTY

### FDA Proposes Changes To Clarify Patent Listing Requirements and 30-Month Stays of Approval Following Submission of Abbreviated New Drug Applications

#### Proposed Changes, If Enacted, Will Substantially Alter the Playing Field for Big Pharma and Generic Drug Companies

The United States Food and Drug Administration (FDA) has proposed amendments to its patent listing requirements for new drug applications (NDAs). The proposal, which was published in the *Federal Register* on October 24, 2002, attempts to clarify the types of patents that must and must not be listed in the FDA's "Orange Book" (formally titled *Approved Drug Products with Therapeutic Equivalence Evaluations*) and proffers revisions to the declaration that NDA applicants must provide regarding their patents, with the aim of ensuring that NDA applicants list only appropriate patents. The proposal would also revise the regulations regarding the effective date of approval for certain applications submitted under section 505(b)(2) of the Federal Food, Drug and Cosmetic Act (FFDCA).<sup>1</sup> In certain situations, Federal law bars the FDA from making the approval of an ANDA<sup>2</sup> or § 505(b)(2) application<sup>3</sup> effective for 30 months if the ANDA applicant certified that the patent claiming the drug is invalid or will be infringed, and the patent owner or NDA holder brings suit for patent infringement. The proposal also states that there will be only one opportunity for a 30-month

<sup>1</sup> Title 21, United States Code

<sup>2</sup> An ANDA is the abbreviation and well-known term for an Abbreviated New Drug Application as codified in § 505(j). An ANDA contains data which, when submitted to FDA's Center for Drug Evaluation and Research, Office of Generic Drugs, provides for the review and ultimate approval of a generic drug product. Generic drug applications are termed "abbreviated" because they are generally not required to include preclinical (animal) and clinical (human) data to establish safety and effectiveness. Instead, generic applicants must scientifically demonstrate that their product is bioequivalent (*i.e.*, performs in the same manner as the innovator drug).

<sup>3</sup> A § 505(b)(2) application is one for which one or more of the investigations relied upon by the applicant for approval "were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted" (21 U.S.C. 355(b)(2)). A § 505(b)(2) application may rely on published literature and/or the Agency's finding of safety and effectiveness for an approved drug.

stay in the approval date of each ANDA or § 505(b)(2) application. According to the FDA, these proposals are designed to make the patent listing process more efficient and to enhance the ANDA and § 505(b)(2) application approval process.

The impetus for these proposed changes arose out of a Federal Trade Commission (FTC) Citizen Petition requesting clarification of several patent listing issues. In July 2002, the FTC issued the results of a comprehensive study of generic drug competition entitled “Generic Drug Entry Prior to Patent Expiration: An FTC Study.” The FTC Study focused on the procedures used to facilitate a generic drug’s entry into the market before the expiration of a patent or patents that pertain to the brand-name drug product.

### Description of the Proposed Rule

The FDA’s proposed rule is intended to assist NDA applicants and NDA holders to determine whether specific patents must be submitted to the FDA for listing and to help § 505(b)(2) application applicants, ANDA applicants, and other interested parties to determine whether a patent listing in the Orange Book is proper. The FDA’s proposed rule would make significant changes to the FDA’s existing regulation governing submission of patent information in New Drug Applications (21 C.F.R. § 314.53). The FDA’s proposed rule addresses:

- the types of patents that must and must not be listed;
- the patent certification statement that NDA applicants must submit as part of an NDA, an amendment to an NDA, or a supplement to an NDA; and
- the 30-month stay in effective dates of approval for a 505(b)(2) application or an ANDA.

The publication of the proposed rules in the October 24, 2002 *Federal Register* provided a 60-day period for the submission of written comments by interested parties. Each of the above proposals will now be discussed in sequence as follows:

#### I. Patent Listing Requirements

Under the FFDCA, an applicant for a new drug shall file with the application the patent number and the expiration date of 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.<sup>4</sup> In spite of this, there has been a prevalence of listing all sorts of patents by innovator companies as part of their effort to retain exclusivity for their products and to prevent generic entry into the marketplace. Numerous examples of this practice were described in great detail in the July 2002 FTC Study.

In addition to patents which claim the drug itself and patents which

claim a method of using such drug, the FDA’s present proposal on patents for which information *must* be submitted includes the following:

- Product-by-Process patents
- Patents that claim different forms of a drug substance than are in the approved drug product, but that would be considered “same” active ingredient for ANDA approval purposes

The proposal on patents for which information *must not* be submitted includes:

- Patents on metabolites
- Patents on intermediates
- Patents on product packaging

#### II. Proposed Changes in the Declaration Requirement Upon Listing a Patent in the Orange Book

- NDA holders would be required to submit declarations for drug substance patents, in addition to patents for drug products and method of use patents.
- NDA holders would be required to identify pending or approved uses claimed by method of use patents.
- The proposed declaration would include a checklist to guide the analysis of the appropriateness of the listing.
- For drug substance patents that claim forms of drug substances that are different from those in the approved drug product, the NDA holder would be requested to state whether an ANDA could be approved for the patented form of the drug substance.

<sup>4</sup> § 505(b)(1) of the FFDCA

### III. 30-Month Stay

When an ANDA is submitted to the FDA for approval, the ANDA filer is required to make one of four certifications under 21 C.F.R. § 505(b)(2) as follows:

1. That no patent on the drug product has been filed for listing in the Orange Book
2. That such patent is expired
3. That the ANDA filer will wait until the patent expires before marketing the generic
4. That the patent is invalid and/or will not be infringed by the manufacture, use or sale of the drug for which the ANDA has been filed (this is known as a “Paragraph IV Certification”)

The 30-month stay provisions are intended to give NDA and patent holders an opportunity to enforce their intellectual property rights prior to approval and market entry of generic drugs. When the patent holder has been properly notified that a Paragraph IV Certification has been made and the patent holder disagrees with the assertions made therein, the patent holder has 45 days to initiate a lawsuit seeking a declaration that the patent is infringed and not invalid.<sup>5</sup> The initiation of a lawsuit by the patent holder entitles said patent holder to a 30-month stay during which the final approval of any ANDA or 505(b)(2) application may not be granted.<sup>6</sup> The 30-month stay period applies unless the court reaches a decision earlier in the patent infringement case or otherwise orders a longer or shorter period for the stay.

In response to comments to the July 2002 FTC Study, the FDA has proposed to change its regulations pertaining to the 30-month stay upon the filing of an ANDA. Previously, the FDA had taken the position that the statute supported having a 30-month stay period for *each* notice of Paragraph IV Certification that led to a patent infringement suit brought within 45 days. The FDA now proposes to change its regulations to limit the applicability of 30-month stay periods to one per ANDA or 505(b)(2) application by the following:

- The FDA requires a patent notice to be sent by the ANDA or 505(b)(2) applicant to the patent holder and the NDA holder only if no previous patent notice had been sent for that application.
- The FDA takes the position that there would not be a 30-month period unless there was a notice of Paragraph IV Certification.

### What the Future May Hold

The Hatch-Waxman Act (formally known as the *Drug Price Competition and Patent Term Restoration Act of 1984*) was intended to balance the competing interests of the pioneer pharmaceutical and allied research-based products industries with those of the generic drug industry. On the one hand, the law responded to the needs of ethical research-based pharmaceutical and related industries to restore patent life lost during the product marketing approval processes of the FDA and other federal agencies. On the

other hand, provisions of Hatch-Waxman responded to the needs of the generic drug manufacturers by providing relief from FDA compliance with the full requirements for conducting clinical studies associated with NDAs as a condition of pre-market approvals for generic copies of “post-1962” drugs, which must be safe and effective (prior to 1962, drugs were approved for safety only). The FDA believes that the present proposals work to preserve the balance struck in the Hatch-Waxman Act and its subsequent amendments between encouraging innovation and encouraging the availability of generic drugs.

Nevertheless, generic companies have long complained that Big Pharma (the pioneer drug companies who are usually the NDA and/or patent holders) have an upper hand because of “loopholes” in the Hatch-Waxman Act—loopholes which have afforded Big Pharma a variety of mechanisms by which to thwart generic drug entry into the market, and which thus incited the aforementioned FTC Study, as well as the FDA’s proposed changes to its patent listing requirements and the 30-month stay provision of the Hatch-Waxman Act.

It remains to be seen whether, and in what form, the above-discussed proposed changes will issue as a final rule. The original Hatch-Waxman Act and subsequent amendments to the Act took many years before being enacted. Should the FDA’s proposed changes be finally issued

<sup>5</sup> § 505(c)(3), FFDCA

<sup>6</sup> §§ 505(c)(1); 505(j)(1), FFDCA

in a form identical to, or very similar to, the present proposals, such changes may be perceived to level the playing field a bit more for generic drug manufacturers since the number of notifications required to be sent to NDA/patent holders will be reduced, and since each NDA/patent holder will be entitled to only a single 30-month stay per ANDA filed which recites the approved drug product or an approved use of the drug. In such an event, the Big Pharmas (who are certain not to be happy with the new requirements) will likely become a bit more cautious and will be prompted to make well-considered representations in their patent declarations, and will

be required to comply with the patent listing requirements so as not to thwart generic drug entry into the marketplace through the use of multiple 30-month stays.

As this Client Advisory went to press, a contact in the Office of General Counsel at the FDA communicated that fewer than 40 written comments were submitted in response to the publication of the proposed rules in the *Federal Register*. These comments, by both innovator drug companies and generic drug companies (and those who represent them), espouse a broad spectrum of views supporting and contesting the FDA's proposals. Furthermore, the Office of General

Counsel at the FDA could not provide any timeline as to when potential changes to the original proposals would be made or when the proposals would issue as a final rule.

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*If you would like further information about the topic covered in this Alert, or any Intellectual Property issue, please contact the Mintz Levin attorney who ordinarily handles your legal affairs, or the attorney author:*

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