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Intellectual Property Update

To Be Listable in the FDA's "Orange Book," Patents Must Recite the API in Claims

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The United States Court of Appeals for the Federal Circuit recently rendered a decision that will significantly impact holders of drug delivery device patents and related technologies. In the precedential decision of *Teva Branded Pharmaceutical Products R&D, Inc. v. Amneal Pharmaceuticals of New York, LLC*, No. 2024-1936 (Fed. Cir. Dec. 20, 2024), the court held that to be listable in the FDA's "Approved Drug Products With Therapeutic Evaluations," a.k.a. "Orange Book," the claims of the patent must recite the active pharmaceutical ingredient (API) of the corresponding FDA approved drug. The Federal Circuit affirmed the district court's order delisting Teva's patents from the Orange Book, since those patents claimed inhalers and components of inhalers, but did not recite the API, albuterol sulfate.

Patents relating to pharmaceutical technologies occupy a unique position at the intersection of patent law and FDA law. Patent law standards, such as the tests for patentability and infringement, apply to pharmaceutical technology patents just as they do to patents in all other technological fields. However, there are regulatory considerations that are unique to the pharmaceutical field, which impact how certain patents in the field are enforced under a statute known as the "Hatch-Waxman Act." One notable aspect of Hatch-Waxman is that certain types of pharmaceutical technology patents must be listed in the Orange Book. Orange Book listed patents are especially powerful for branded pharmaceutical companies since they can be used to impede FDA approval of generic versions of branded drugs, even before a court makes a substantive infringement determination.

In the United States, a pharmaceutical company that seeks to market a new drug must submit a New Drug Application (NDA) that sufficiently demonstrates the safety and efficacy of the drug to merit FDA approval. Once an NDA is approved, information about the approved new drug is set forth in the Orange Book. The Orange Book entry for a given drug, among other things, must identify "the patent number and expiration date of each patent for which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug, and that … claims the drug for which the applicant submitted the application …". 21 U.S.C. § 355(b)(1)(A)(viii). The statute, as recently amended in the Orange Book Transparency Act ("OBTA"), Pub. L. No. 116-290, 134 Stat. 4889 (2021), further requires that the listed patent "is a drug substance (active ingredient) patent or a drug product (formulation or composition) patent; or … claims a method of using such drug for which approval is sought or has been granted in the application." 21 U.S.C. § 355(b)(1)(A)(viii). It is the NDA sponsor's responsibility to submit such patent information. The FDA, which is said to have only a "ministerial" role in receiving patent information from the sponsor, does not police patent listings. Thus, if the NDA sponsor submits a patent for listing in the Orange Book, it is listed as a matter of course.

A company that wishes to enter the market with a generic version of the NDA drug must submit an Abbreviated New Drug Application (ANDA). The ANDA can piggyback off the safety and efficacy data in the NDA so long as the ANDA applicant can demonstrate that the proposed generic is bioequivalent to the branded drug. If an ANDA filer wants to start the approval process during the term of any listed patents but does not seek to obtain approval until after the patents are expired, the ANDA filer may submit a "Paragraph III certification." Such a path would not give rise to a cause of action for infringement. However, if the ANDA filer wants to obtain marketing approval prior to expiration of

the Orange Book listed patents, the ANDA filer must represent, through a "Paragraph IV certification," that the proposed generic version would not infringe the patents and/or that the patents are invalid or unenforceable. Upon receiving notice of a Paragraph IV certification, the NDA holder may sue the ANDA filer within a designated time (45 days) to enforce one or more of its Orange Book listed patents with the objective of preventing, or at least slowing down, generic entry into the market. Since the act that gives rise to the infringement lawsuit is the mere filing of the ANDA and Paragraph IV certification (i.e., before any commercial launch of the generic), the Hatch-Waxman statute "is designed to create an artificial act of infringement for purposes of establishing jurisdiction in the federal courts."[1]

A lawsuit under Hatch-Waxman automatically triggers a statutory thirty-month stay on FDA approval of the generic drug, regardless of the merits of the infringement case. This is a unique remedy that does not exist in patent law outside of the ANDA infringement context. The thirty-month stay effectively operates as a de facto preliminary injunction against the ANDA applicant, allowing the NDA holder to maintain its market exclusivity while the infringement and/or invalidity case proceeds through the courts. An Orange Book listable patent is thus a crucial tool for a branded drug company to protect its market exclusivity. However, not all patents relating to pharmaceutical technologies are listable in the Orange Book.

In *Teva v. Amneal*, the NDA sponsor, in this case Teva, had submitted an NDA for its ProAir® HFA Inhalation Aerosol, which is an inhaler device that administers albuterol sulfate for treatment or prevention of bronchospasm with reversible obstructive airway disease. Teva listed nine non-expired patents in the Orange Book, five of which were relevant to the case. Those five patents all related to improvements in the inhaler device components, particularly the dose counter. Notably, none of the five patents included claims reciting an active drug. The question was whether these device patents were properly listed in the Orange Book due to this alleged deficiency. If the listings were improper, then the patents would be delisted.[2] This would, in turn, have the effect of lifting the automatic thirty-month stay of FDA approval, clearing the path for early approval and launch of Amneal's generic version of the inhaler.

The Federal Circuit had to determine whether, under the Hatch-Waxman Act, a patent "claims the drug for which the applicant submitted the application," when: (a) the patent's claims cover or "read on" the accused product (Teva's position); or (b) only when the patent claims explicitly recite the API (Amneal's position). After a detailed statutory interpretation analysis, the court announced the following holding:

> [T]o qualify for [Orange Book] listing, a patent must claim at least what made the product approvable as a drug in the first place – its active ingredient. In other words, Teva cannot list its patents just because they claim the dose-counter and canister parts of the ProAir® HFA.[3]

The patents at issue in *Teva* relate to products that may be characterized as drug delivery devices or drug-device combinations. Teva argued that since its ProAir® HFA was approved as a drug via the NDA pathway, even the components of the inhaler should be statutorily part of the approved "drug," rendering patents covering those components Orange Book listable. The court was unpersuaded. The Federal Circuit concluded:

> [A] drug-device combination product being approved with an NDA does not make the device parts a drug. The fact that the combination product was approved with an NDA just means that the drug mode of action predominated. On the facts of this case, the drug for which the application was submitted and approved is thus not every component of Teva's ProAir® HFA.

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[1] *Glaxo Group Ltd. V. Apotex, Inc.*, 376 F.3d 1339, 1351 (Fed. Cir. 2004) (emphasis in original).
[2] *See* 21 U.S.C. § 355(j)(5)(C)(ii)(I), which enables a generic drug company in a Hatch-Waxman lawsuit to file a counterclaim to delist Orange Book patents that were allegedly improperly listed.
[3] *Teva Branded Pharmaceutical Products R&D, Inc. v. Amneal Pharmaceuticals of New York, LLC*, 2024 WL 5176737 at *8 (Fed. Cir. Dec. 20, 2024)

> Instead, it is the part of the drug-device combination that made it regulatable as a drug in the first place. And that is the active ingredient.[4]

It appears that the outcome of this case could have been completely different had there been one seemingly slight change in the patents-at-issue. Had each of those patents included even a single dependent claim reciting, e.g., "the medicament canister containing therein a medicament in the form of an aerosol, the medicament comprising albuterol sulfate," it would seem that the patents would have been Orange Book listable.

In view of the court's holding in *Teva*, branded pharmaceutical companies and companies who develop and patent drug delivery devices should consider the following:

To the extent that the company has existing Orange Book patent listings, review those patents to confirm that they each include at least one claim explicitly reciting the active pharmaceutical ingredient of the approved drug.

If patents for the device do not currently recite active pharmaceutical ingredients in the claims, review the disclosure and status of the patents to determine whether corrective measures may be utilized to render those patents, or perhaps related patents, compliant with Orange Book listability requirements. This may include, for example, considering any disclosures that were incorporated-by-reference into the patents that may describe the approved drug and/or filing continuations, continuations-in-part, re-examinations, reissues or new applications (e.g., for improvements on the device and to include claims reciting the relevant API(s)) to address the problem.

Remember that drug delivery devices are more than sophisticated mechanical inventions. They are platforms for delivering drugs and could be Orange Book listable if drafted to include the relevant drug(s) in the claims. For this reason, some drafters of these patents consciously include the intended or likely drug(s) to be used with the device. In some cases, patent drafters may go so far as to include lengthy lists in the patent's specification of potential drugs that may be delivered using the patented device. Such lists or portions of them may be recited in the patent's claims, e.g., in "Markush" format.

A close read of *Teva* and an understanding of its implications will allow drafters of patents for drug-device combinations to better position their clients' patent portfolios for effective licensing and enforcement, while at the same time avoiding risks associated with improper Orange Book listing. Such risks include delisting, potential antitrust liability, and possible Federal Trade Commission scrutiny.

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[4] *Id*. at *16.