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Overcoming Restriction Requirements On Pharma Patents

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Patent prosecutors strive to optimize protection afforded by pharmaceutical patents for branded pharmaceutical clients. For reasons discussed herein, one underappreciated way to optimize pharmaceutical patent protection is to successfully address a restriction requirement (or lack of unity of invention counterpart) raised by a U.S. Patent and Trademark Office examiner during a patent examination.

Restriction occurs when, in the opinion of the USPTO, there are at least two inventions in a single patent application and (i) the inventions are independent or distinct and (ii) there would be a serious burden on the examiner if restriction is not required.[1] The effect of a restriction requirement, if made final and not withdrawn, is that at least one invention will not be examined. The nonexamined invention can be separately pursued in a divisional application.[2]

Overcoming a USPTO restriction is not trivial. Attempts to overcome a restriction can produce more prosecution history estoppel than simply not traversing. Additionally, because restricted claims can be separately pursued in follow-on applications, accepted thinking is often that one patent that includes claims to both a drug product and methods of making the drug is essentially equivalent to two patents — the first containing claims to a drug and the second containing claims to methods of making the drug. For some or all of these reasons, patent practitioners may choose not to contest a restriction requirement.

The thinking that one patent contains two types of claims (e.g., drug product and methods of making the drug) is "about equal" to two patents each containing one claim (e.g., a drug patent and a method of making the drug) is upset by Orange Book listing rules. From Orange Book and subsequent pharmaceutical patent litigation lenses, the single patent containing two claim types can provide significantly more value.

The Orange Book

The Orange Book[3] contains a listing of drugs approved by the U.S. Food and Drug Administration under the Federal Food, Drug and Cosmetic Act. The Orange Book, among other things:

- Lists periods of market exclusivitie(s) associated with drug approvals;
- Lists U.S. patent numbers associated with drugs and their expiration dates; and
- Provides use codes for patents having method of treatment claims.

Orange Book Listing Rules

Patents eligible for Orange Book listing must be timely filed.[4] And, only patents containing at least one claim to the approved:

(i) Drug substance (active ingredient) — including some polymorphs,
(ii) Drug product (formulation and composition) and
(iii) Method(s)-of-use,

qualify for Orange Book listing.[5] In contrast, "[p]rocess patents, patents claiming packaging, patents claiming metabolites and patents claiming intermediates are not covered ... and information on these patents must not be submitted to the FDA." Thus, the only way to get issued claims to methods of making a drug, intermediates used therein and drug metabolites, into the Orange Book is to have those "unlistable" claims issue in a patent also containing at least one Orange Book listable claim.

Contesting a Restriction Requirement — An Alternative Strategy

It is not unusual for a restriction requirement to be issued by a USPTO examiner, which forces a patentee to choose between:

- A drug;
- A key intermediate for making the drug;
- Methods of making the drug;
- A drug metabolite; and
- Methods of treating patients using the drug.[6]

Because drug patent claims are generally perceived to be valuable, these are often selected when responding to a restriction requirement. If restriction is maintained, the resulting patent will issue containing only drug claims and this drug patent will end up being Orange Book listed. Claims to the remaining inventions, excluding methods of treating patients with the drug, are pursued in separate divisional patents that are not Orange Book listable. But where a restriction requirement is successfully traversed or rejoinder[7] is requested and affected, the Orange Book listed patent will contain additional, diverse, claims drawn to potentially include key intermediates for making the drug, methods of making the drug and a drug metabolite.

Implications of Diverse Orange Book Listed Claims

The process of commercializing a generic drug begins by reviewing Orange Book listed patents for the branded drug. If the intent is to file an abbreviated new drug application, or ANDA, before Orange Book listed patents expire, the would-be ANDA filer then usually obtains opinions from patent counsel as to why the patents are not infringed, invalid or unenforceable.[8] Positions taken in the opinions form the basis for the notification letter that is legally required to be sent to the branded patent holder after the ANDA is filed by the FDA. Filing of an ANDA is an infringing act[9] and the branded patent holder, after

receiving notice, is provided the opportunity to sue the ANDA filer in a federal district court, thereby triggering an automatic 30-month stay in ANDA approval.

Having a diversity of claims in Orange Book listed patents creates significant added barriers to would be generic manufacturers. For example, because the diverse claims are Orange Book listed, a 30-month stay of FDA approval can be based upon these claims. In the absence of having these diverse claims Orange Book listed, a patentee would need to take additional action, for example attempting to get a preliminary injunction based on diverse claims not found in the Orange Book listed patent(s).

Also, the inclusion of diverse claims can force the generic manufacturer to take invalidity or noninfringement positions earlier-in-time than they may otherwise would. Opinions for non-Orange Book listed claims can be finalized later in time — because of the notification and lawsuit timelines — than those for Orange Book listed claims. Formulating invalidity positions that can survive challenge takes time and rigorous thinking. Given time pressures associated with opinions and related ANDA filings, some of these positions may end up being rushed, may be suboptimal, and therefore, may be more open to successful rebuttal by the branded drug patent holder. The ANDA filer may then feel pressure to move away from these initial positions to new legal theories during litigation. Doing so can be more likely to result in sanctions and fee shifting — which can easily run into millions of dollars.[10][11][12]

Dealing with Restriction Requirements

Successfully addressing restriction requirements can improve the protection afforded by pharmaceutical patents. While each restriction requirement is unique and must be treated as such, potential ways to increase the odds of having more diverse Orange Book listed claims include:

- Attack mere assertions that the claims are distinct. In some instances, patent examiners will merely assert that claims to two or more inventions are distinct without providing a reasonable basis for this conclusion. In these instances, arguing that the patent examiner has not met the legal burden for showing restriction is necessary may overcome the requirement.

- Argue no serious burden. In cases containing small numbers of claims of relatively consistent claim scope, it may be possible to persuade a patent examiner through reasoned argument that examining all claims would not represent a serious burden.

- Call out misconstruing of special technical features and mischaracterization of applied references. Doing so can overcome some unity of invention rejections.

- Ask for rejoinder where appropriate.

- Make judicious use of product by process claims. If a requirement is sustained and a follow on application is filed with claims drawn to methods of making a drug, patent examiners may allow inclusion of dependent product-by-process claim(s). Because product-by-process claims which cover the drug are Orange Book listable, inclusion of one of these claims can allow method-of-making claims to be Orange Book listed.[13]

Conclusion

Restriction requirements (and lack of unity of invention equivalents), if not challenged and overcome, can decrease the claim diversity of Orange Book listed patents and smooth the allowance pathway for generic manufacturers. At multiple levels, overcoming restriction requirements provides advantages for protecting pharmaceuticals. Addressing restriction requirements (and lack of unity of invention equivalents) should therefore be given appropriate attention.

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The authors dedicate this article to Peter Munson — friend, colleague, mentor, lawyer, scholar, Renaissance man. You are and will be missed.

[1] See, e.g., M.P.E.P. § 803.

[2] See, e.g., 35 U.S.C. § 121.

[3] Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations, last accessed July 27, 2015.

[4] To be timely listed, U.S. patents in force at the point of new drug application (NDA) approval must be Orange Book listed within 30 days of approval. See, e.g., 21 C.F.R. § 314.53(c)(2)(R)(ii). “Within 30 days after the date of approval of its application or supplement, the applicant shall submit FDA Form 3542 for each patent that claims the drug substance (active ingredient), drug product (formulation and composition) or approved method of use ... ”

For U.S. patents issuing after NDA approval, “ ... the applicant shall submit to FDA the required patent information within 30 days of the date of issuance of the patent.” 21 C.F.R. § 214.53(d)(2).

[5] See, e.g., 21 C.F.R. § 314.53(b)(1).

[6] A restriction requirement between a drug, a method of treating a disease using that drug and a pharmaceutical formulation of that drug, could be useful as it allows the separation of different Orange

Book categories into putatively patentably distinct patents. It may make sense to not contest that type of restriction requirement. Restriction requirements should be evaluated on a case by case basis as part of a general patent strategy.

[7] See, e.g., M.P.E.P. § 821.04.

[8] See, e.g., D. Hoffmeister, V. Norviel, J. Guise, P. Munson, S. Williams, D. Carsten, R. Torczon, and P. Girinath, "Takeaways for Generics After Octane and Highmark," Law360, September 15, 2014.

[9] See 35 U.S.C. § 271(e)(2).

[10] See, e.g., Yamanouchi Pharmaceutical Co. Ltd. v. Danbury Pharmacal Inc., 231 F.3d 1339 (Fed. Cir. 2000).

[11] For an example of method of making claims keeping generics off the market, see e.g., Albany Molecular Research Inc. v. Dr. Reddy's Laboratories Ltd. et al., case number 09-cv-4638; and Albany Molecular Research Inc. v. Sandoz Inc. et al., case number 09-cv-4639; both in the U.S. District Court for the District of New Jersey

[12] Examples of drugs that that have Orange Book listed patents containing diverse claims include rivaroxaban and sofosbuvir.

[13] When deciding to include product-by-process claims, consider the possibility that doing so may result in loss of divisional application safe harbor status and the implications thereof.