IPI
International Pharmaceutical Industry

Volume 14 Issue 2

Peer Reviewed

Annex 1
Implementation of the Final Draft

Applying Advanced Powder Testing to
Tackle the Toughest Formulation Challenges

Achieving Faster Investigational New Drug Timelines with a
Robust Cell Line Development Strategy

Shared Care
Strengthening Self-management Support for Chronic Patients

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Latest Developments in IP Strategies for Pharmaceuticals

The strategies used to create and maintain strong pharmaceutical patent portfolios must evolve with developments in the pharmaceutical space. These developments include not just scientific advancements but also requirements and practices of regulatory bodies, such as the United States Food and Drug Administration (FDA). This article addresses innovative prosecution strategies and useful considerations that may facilitate better agreement between pharmaceutical patent practice and FDA policy.

Means-Plus-Function Claiming

Rooted in the principle that bioequivalent products need not undergo duplicative testing to get to market, US regulatory law offers two routes to accelerated FDA approval that rely, at least in part, on studies conducted by an earlier innovator. One route is the abbreviated new drug application (ANDA) pathway (for small molecule drugs) or abbreviated biologics license application (aBLA) pathway (for biologics). The other is the 505(b)(2) pathway. The ANDA and aBLA pathways typically require that the applicant use the same active agent(s) in their product as used in the innovator's product, while the 505(b)(2) pathway permits more variation, including in dosage form or regimen, route of administration, or even new active ingredients.

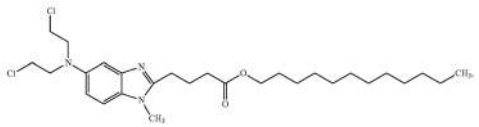
However, these pathways also highlight a mismatch between US regulatory law and patent law. For example, the level of equivalence appropriate for accelerated US regulatory review, particularly under 505(2)(b), is often broader than the scope of an innovator's patent claims as assessed under literal infringement. Moreover, the doctrine of equivalents can be greatly restricted by, for example, prosecution history estoppel, increasing the likelihood of design-arounds that significantly reduce an innovator's patent exclusivity.

Means-plus-function claims, under 35 U.S.C. § 112(f), may better harmonise patent prosecution strategy with FDA practice. These claims define an element, in a combination claim, by its function instead of its structure. Importantly, means-plus-function claims guarantee a scope of equivalence that is independent from the scope provided under the doctrine of equivalents and is not subject to the same prosecution history-based estoppels as the doctrine of equivalents. Instead, means-plus-function claims cover equivalents to "the corresponding structure, material, or acts described in the specification."[2]

There are two basic types of means-plus-function claims in the pharmaceutical space. The first type recites (a) a structure-defined composition, and (b) a means for achieving a desirable outcome. In pharmaceutical inventions, such a claim commonly recites a specified active agent and a "means" for improving delivery, stability, or bioavailability of the active agent. In other words, the "means" is typically a function-limited pharmaceutically acceptable excipient. Examples of this type of claim appear below:

This first type of means-plus-function claim may prove valuable against an ANDA or aBLA applicant, who would necessarily use the same active agent claimed by the innovator but might seek approval for an alternative formulation compared to the innovator's product and formulation claims. While a showing of bioequivalence is required for ANDA or aBLA approval, it might not suffice for a finding of infringement under the doctrine of equivalents. By contrast, infringement of a "means" term, which includes statutory functional equivalents, may be evidenced by the same showing of bioequivalence required by the FDA. Thus, a means-plus-function claim may provide an innovator with more comprehensive protection of their invention by bridging the gap between FDA practice and patent law.

The second type of means-plus-function claim may prove valuable against a 505(b)(2) applicant or a competing innovator. As exemplified below, the second type of means-plus-function claim is characterised

U.S. Patent No.	Means-plus-Function Claim (First Type)
9,149,464	13. A pharmaceutical composition, comprising (a) a compound of which is 4-5{-[bis-(chloroethyl)-amino]-1-methyl-1H-benzimidazol-2-yl}butyric acid dodecyl ester having the chemical structure:  or a pharmaceutically acceptable salt thereof, and (b) a means for increasing the circulation time of the compound in an aqueous environment.
10,413,611	1. A pharmaceutical composition comprising: (a) at least one poloxamer selected from poloxamer 124, poloxamer 188, poloxamer 237, poloxamer 338, and poloxamer 407, or a mixture thereof; and (b) means for keeping the pharmaceutical composition in liquid phase up to a temperature of about 40° C. *in vitro*, wherein the pharmaceutical composition is for use in submucosal lift of gastrointestinal mucosal lesions in a patient undergoing a gastrointestinal endoscopic procedure.
7,579,380	20. A pharmaceutical composition, comprising at least one core which is surrounded by at least one osmotic subcoat, at least one control-releasing coat which surrounds the at least one osmotic subcoat, wherein the at least one core comprises bupropion hydrobromide and at least one excipient, wherein the at least one osmotic subcoat comprises at least one osmotic agent and at least one osmotic deposition vehicle, and a means for releasing the bupropion hydrobromide from the composition.

by (a) a means term that describes the function of an active agent, and (b) a second component (e.g., an excipient). In *Ex parte Gleave*,[3] the Patent Trial and Appeal Board (PTAB) reversed an examiner's rejection of such a means-plus-function claim, which ultimately granted as claim 9 in US Patent No. 8,722,872:

U.S. Patent No.	Means-plus-Function Claim (Second Type)
8,722,872	9. A pharmaceutical composition comprising a (a) means for reducing the amount of active hsp27 in cancerous cells and (b) a pharmaceutically acceptable carrier.

The PTAB found that the means-plus-function claims were proper and summarised the scope of the recited "means" term based on support in the specification:

We agree with Appellants that the structures disclosed in the Specification as having the function recited in the claims are limited to (a) the specific antisense oligonucleotides in Example 1, (b) the specific RNAi molecules of Example 5, and (c) equivalents thereof, that are effective in reducing the amount of hsp27 in cancerous cells.[4]

Again, "equivalents," as used in this context, include statutory functional equivalents, and do not implicate the stricter standards of the doctrine of equivalents. Therefore, a "means" term that characterises an active agent may enhance patent protection against design-arounds that exchange the innovator's drug with an alternative having equivalent therapeutic properties.

By encompassing statutory equivalents of the claimed subject matter, means-plus-function claims can prevent competitors from designing around an invention by making a change to a drug composition or combination that is not expressly recited in an innovator's claims but would still qualify for accelerated approval under current FDA practice. As such, means-plus-function claims can be a powerful tool when drafting pharmaceutical claims to encompass broader claim scope and thus more fully protect an inventor's rights and provide greater protection against infringement.

We note, however, that pharmaceutical patents containing means-plus-function claims have rarely been considered by the PTAB or the courts. Thus, while it may be possible to obtain a patent containing means-plus-function claims, such patents could attract challenges in post grant proceedings and/or litigation. We, therefore, recommend pursuing such claims in patent applications that clearly define the scope of the means term in the specification, such as through a definition, a detailed description of embodiments, or a table linking the means term to its intended scope. This approach may provide patent owners with greater confidence surrounding the scope and enablement of their means-plus-function claims.

We also note that means-plus-function claims may be interpreted differently, if allowed at all, outside of the US. Certain jurisdictions disfavour claim terms defined by function rather than structure, even with strong support in the specification as to the scope of those terms. Moreover, patent laws guiding the interpretation of equivalents to a claimed feature can differ significantly across jurisdictions and can be inconsistently applied. Thus, the protective scope of means-plus-function claims outside of the US will likely vary by country and court.

Claiming the Label ("*Sanofi v. Watson*" Claiming)

As alluded to above, the ANDA pathway allows a generic company to rely on an innovator company's studies to obtain FDA approval for their generic product, thus potentially accelerating its entry into the market. Similarly, through the aBLA pathway, a biosimilar company may rely on innovator data to accelerate FDA approval of its biosimilar product. With limited exceptions, the generic or biosimilar drug must carry the same label information provided in the label for the innovator's drug.[5] While the FDA does allow a generic or biosimilar label to differ from an innovator's label by omitting a feature protected by patent exclusivity, the innovator can use strategic patent claiming to limit the applicability of this exception.

The 2017 Federal Circuit decision in Sanofi v. Watson[6] illustrates that an innovator can use patent claims that closely correspond to their drug label language to provide extended protection against generic or biosimilar products.

As summarised in the Sanofi decision, Sanofi claimed certain Phase III clinical trial results of its drug Multaq® (dronedarone) in its US Patent No. 8,410,167. The Multaq® label included the same clinical trial results recited in the '167 patent claims, both explicitly and by reference to the underlying Phase III study. The similarities in Sanofi's claim and label language are depicted in the table below:

US Patent No. 8,410,167, Claim 1	Multaq® Label
1. A method of decreasing a risk of cardiovascular hospitalisation in a patient, said method comprising administering to said patient an effective amount of dronedarone or a pharmaceutically acceptable salt thereof, twice a day with a morning and an evening meal, wherein said patient does not have severe heart failure, (i) wherein severe heart failure is indicated by: a) NYHA Class IV heart failure or b) hospitalisation for heart failure within the last month; and (ii) wherein said patient has a history of, or current, paroxysmal or persistent non-permanent atrial fibrillation or flutter; and (iii) wherein the patient has at least one cardiovascular risk factor selected from the group consisting of: i. an age greater than or equal to 75; ii. hypertension; iii. diabetes; iv. a history of cerebral stroke or of systemic embolism; v. a left atrial diameter greater than or equal to 50 mm; and vi. a left ventricular ejection fraction less than 40%.	INDICATIONS AND USAGE MULTAQ is an antiarrhythmic drug indicated to reduce the risk of cardiovascular hospitalisation in patients with paroxysmal or persistent atrial fibrillation (AF) or atrial flutter (AFL), with a recent episode of AF/AFL and associated cardiovascular risk factors (i.e., age >70, hypertension, diabetes, prior cerebrovascular accident, left atrial diameter ≥50 mm or left ventricular ejection fraction [LVEF] <40%), who are in sinus rhythm or who will be cardioverted (1,14). DOSAGE AND ADMINISTRATION One tablet of 400 mg twice a day with morning and evening meals (2)... CONTRAINDICATIONS Class IV heart failure or symptomatic heart failure with a recent decompensation (Boxed Warning, 4) ...

Defendants, Watson Laboratories Inc. and Sandoz Inc., filed ANDAs with the FDA, requesting approval to market generic versions of Multaq®. In compliance with FDA policy, Watson and Sandoz proposed essentially copying the Multaq® label for their generic drug label, including relying on the same clinical study data and information described and referenced in the Multaq® label. The Federal Circuit found that the defendants' generic label provided sufficient basis for a finding of "intentional encouragement of infringing use and, therefore, of inducement" to infringe the '167 patent claims.[7]

This decision reveals that, by "claiming the label," an innovator can leverage their knowledge of FDA procedure to force generic or biosimilar companies into induced infringement, and thus into a choice between early market entry and freedom to operate.[8]

A caveat to this strategy is the prior art effect of published clinical trial protocols and data. Therefore, patent teams should coordinate early and frequently with regulatory teams to ensure that innovators file their patent applications before any upcoming clinical trial disclosures, or at least within the grace period permitted under US law.

We also caution that this strategy may not find similar success outside of the US. In certain jurisdictions, local patent laws may prohibit features like dosages, dosing regimens, and patient subpopulations from carrying patentable weight. And other jurisdictions may not permit medical treatment or use claims under any circumstances. Further, grace periods outside of the US tend to be less generous, if they exist at all, making coordination of these patent application filings and clinical trial disclosures a greater challenge. Thus, it may not be feasible to draft claims that track drug label language in all jurisdictions.[9]

Conclusion

The claim strategies discussed herein provide pharmaceutical inventors with additional tools to achieve meaningful patent protection for their inventions in the US. By drafting claims to track the FDA-approved label via "Sanofi v. Watson" claiming, pharmaceutical patent owners can improve their chances of establishing induced infringement. And by pursuing means-plus-function claims, pharmaceutical patent owners may be able to more fully protect against obvious design-arounds. These techniques, which align pharmaceutical claim strategy with FDA policy, have enormous potential to more robustly protect an inventor's rights and provide greater protection against infringement.

REFERENCES

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2. The statutory language reads: "An element in a claim for a combination may be expressed as a means or step for performing a specified function without the recital of structure, material, or acts in support thereof, and such claim shall be construed to cover the corresponding structure, material, or acts described in the specification and equivalents thereof." 35 U.S.C. § 112(f).
3. Appeal 2012-004973 (P.T.A.B. Jan. 22, 2014).
4. Id. at *7.
5. See, e.g., 21 U.S.C. 355(j)(2)(C); 21 CFR 314.93; 21 CFR 314.94(a)(8)(iv).
6. Sanofi v. Watson Lab'ys Inc., 875 F.3d 636 (Fed. Cir. 2017).
7. Id. at 646.
8. This claim approach, also used in Sanofi's US Patent No. 10,300,065, not only provided Sanofi with additional protective scope of Multaq® and its use, but also extended Sanofi's patent exclusivity 10 years beyond the term of their composition-of-matter patent. Thus, a potential added benefit of "claiming the label" is to increase the duration of an innovator's patent exclusivity.
9. For further guidance on whether "claiming the label" may be feasible in jurisdictions beyond the US, see Patent Subject Matter Eligibility: A Global Guide (Paul W. Browning et al. eds., 2021), and consult local counsel.

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