Pharmaceutical companies rely heavily on the exclusivity afforded by patents as a strategy for recovering costs associated with drug development and generating profits from new drug sales. In an attempt to balance the rewards of patent protection with the wide-ranging benefits of generic drug availability, Congress passed the Drug Price Competition and Patent Term Restoration Act (Hatch-Waxman Act) in 1984. The “safe harbor” exemption of the Hatch-Waxman Act was intended to provide a narrow exception to patent infringement to facilitate generic drug entry into the market. However, the politically compromised, vague wording of the law has allowed the safe harbor exemption to be interpreted by the courts in ways that would expand the exemption to include a host of activities that Congress likely never intended.

In the 1990 landmark case of Eli Lilly v. Medtronic, the Supreme Court held that the safe harbor exemption applies not only to drugs, but also to medical devices. Moreover, several recent court decisions have interpreted the law’s broad phrases “solely for uses” and “reasonably related” in ways that have further expanded the safe harbor exemption.

Are Post-Approval Activities “Reasonably Related?”

In 2011, the Court of Appeals for the Federal Circuit (CAFC) was asked to rule on whether the safe harbor exemption applied to post-Food and Drug Administration (FDA) approval activities in Classen Immunotherapies v. Biogen. The case focused on U.S. Patent Nos. 6,638,739 (the ‘739 patent), 6,420,139 (the ‘139 patent), and 5,723,283 (the ‘283 patent) assigned to Classen. The ‘739 and ‘139 patents claim methods requiring the steps of “(1) compar[ing] the incidence of chronic immune mediated disease in two groups of mammals who were immunized according to different schedules and then (2) immuniz[ing] a mammal according to the lower risk schedule.” The ‘283 patent claims methods requiring the steps of “(1) immunizing a group of mammals according to a schedule and then (2) comparing the incidence of chronic immune mediated disorder in the group to a control group.” Based on these patented methods, Classen accused Biogen and GlaxoSmithKline of infringing its patents for allegedly participating in post-FDA approval studies “to evaluate suggested associations between childhood vaccinations…and risk of developing type 1 diabetes; and to determine whether timing of vaccination influences risk,” but the district court held that these activities fall within the safe harbor exemption.

Classen appealed to the CAFC, arguing that the safe harbor exemption is limited to activities performed to obtain pre-marketing approval of generic counterparts of patented inventions. The CAFC ruled in favor of Classen, with the majority opinion stating that “§271(e)(1) provides an exception to the law of infringement to expedite development of information for regulatory approval of generic counterparts of patented products” and that “[t]he statute does not apply to information that may be routinely reported to the FDA, long after marketing approval has been obtained.”

Many legal commentators interpreted the Classen decision to mean that the safe harbor exemption would apply only to pre-approval activities, which would be a novel reading of the safe harbor statute and preclude exemption to patent infringement for FDA-ordered post-market review clinical trials.

Closely following Classen was Momenta v. Amphastar, a case between two manufacturers of...
generic enoxaparin that focused on U.S. Patent No. 7,575,886 (the ‘886 patent) assigned to Momenta. The ‘886 patent generally relates to “methods for analyzing heterogeneous populations of sulfated polysaccharides, e.g. heparin [and]...LMWH [e.g., enoxaparin.]” Shortly after Amphastar received FDA approval to market generic enoxaparin (and over a year after Momenta received its own FDA approval to market generic enoxaparin), Momenta sued Amphastar, alleging that Amphastar infringed the ‘886 patent by “manufacturing generic enoxaparin for commercial sale.” Momenta also alleged that the infringing activity was for post-FDA approval requirements and argued that such activities do not fall within the safe harbor exemption, as held in Classen. The CAFC disagreed, stating that Amphastar’s submissions were not “routine submissions” to the FDA, but instead were submissions that were required to maintain FDA approval and that “[f]ailure to comply with these requirements could result in suspension or revocation of Amphastar’s [Abbreviated New Drug Application] ANDA approval to market the drug.” Momenta further contended that the information in question was not “submitted” to the FDA, but rather was only retained by Amphastar for possible FDA review. However, the CAFC stated that “the requirement to maintain records for FDA inspection satisfies the requirement that the uses be reasonably related to the development and submission of information to the FDA.”

In 2013, the Supreme Court asked the Solicitor General to comment on GlaxoSmithKline’s petition for certiorari seeking review of the Classen decision. In light of Momenta, the Solicitor General said there was no reason to review Classen because it was now clear that the Federal Circuit was not limiting the safe harbor to pre-approval activities. Post-approval activities that are reasonably related to the submission of information required by the FDA, fall within the safe harbor exemption.

“Solely for Uses” and Non-Approval Products

In 2008, the CAFC affirmed a district court ruling in Proveris v. Innovasystems that an infringer cannot claim exemption under the safe harbor when the infringing device is not, itself, subject to FDA approval. Proveris is the owner of U.S. Patent No. 6,785,400 (the ‘400 patent), which claims spray characterization devices for characterizing aerosol sprays commonly used in various nasal spray pumps and inhalers. While Proveris’ devices are not themselves subject to FDA approval, the FDA does require characterization data that can be generated by Proveris’ devices for approval of inhaler-based drug delivery devices. In 2005, Proveris sued Innovasystems, alleging that Innovasystem’s Optical Spray Analyzer (OSA) infringed the ‘400 patent. Innova argued that because the OSA was sold exclusively to pharmaceutical companies and the FDA as a research tool that was used only in connection with applications for regulatory approval, the infringing activity was entitled to the benefit of the safe harbor exemption. A district court disagreed with Innovasystems, and on appeal, the CAFC affirmed the district court ruling, stating that because the OSA “faces no regulatory barriers to market entry upon patent expiration… Innova[systems] is not within the category of entities for whom the safe harbor provision was designed to provide relief.”

Teva Pharmaceuticals attempted to rely on the Proveris ruling when filing suit against Sandoz, Inc. and Momenta in 2009 and 2010 for the infringement of so-called biomarker patents. Teva is the exclusive licensee of U.S. Patent Nos. 6,514,938, 7,074,580, 7,163,802, and 7,615,359 (collectively referred to as the “Gad Patents”), which relate to a drug called Copaxone for treating multiple sclerosis. The Gad Patents claim polypeptide markers and methods for using such markers to characterize the active ingredient in Copaxone; however, the claimed markers are not themselves drug products requiring FDA approval. Sandoz and Momenta used methods claimed in the Gad Patents to characterize active ingredients in generic forms of Copaxone to provide required data to the FDA for approval of the generic drugs. These actions triggered Teva to file a suit in reliance on the Proveris decision; however, a district court concluded that Teva read Proveris too narrowly, stating (in reference to Proveris) that “[w]hen a ‘patented invention’ is not used solely for developing information and submission, that invention…is not covered by the safe harbor” and that “[c]ommercialization is a square peg in a round hole.” Acknowledging that Sandoz and Momenta used Teva’s claimed methods solely for uses reasonably related to the development
and submission of information for FDA approval, the district court held that the safe harbor exemption protected those activities.

What Biologic Patent Owners Need to Know

In total, the indefinite language of the safe harbor exemption has significantly increased the uncertainty associated with patent enforceability and ultimately the risk associated with developing new drugs and other medical devices. The Classen and Momenta rulings indicate that the safe harbor exemption applies to post-FDA approval activities to generate information that is required to maintain drug approval. The implications of Momenta are particularly significant for biologic manufacturers who are required to maintain and provide to FDA, batch-by-batch data on drugs being offered for commercial sale. Thus, biosimilar drug manufacturers that use brand process patents in the production of competing drugs appear to be protected by the safe harbor because their production processes are required to be held for FDA inspection. Query whether Momenta can be read even broader to cover all drug manufacturing activities, as these are required to comply with the FDA’s quality system regulation and must be made available for routine FDA inspection.

The Proveris and Teva decisions suggest that commercial sales of non-approval inventions will fall outside the bounds of “solely for uses” related to generating information required by a federal law, but that infringement involving non-approval inventions will be exempted when the activity is performed “solely for uses” related to generating information required for approval of another product. Such fine distinctions among what is considered “solely for uses,” and “reasonably related” can leave drug manufacturers with a discomfoting uncertainty as to which FDA approval activities are in fact “safe.” Trade secrets may provide an alternative form of protection where drug manufacturers feel that relying on patents is too risky.