Protecting New Investments in Old Drugs

by Terry Mahn

In an earlier article, the author discussed the shift taking place since the 2003 Orange Book reforms with pioneer drug companies looking for new ways to protect old drugs. A creative approach followed by some pioneers has been to patent new drug features that would appear on drug labels in the form of patent-protected language that generic manufacturers are then either forced to infringe, await expiration or seek Food and Drug Administration (FDA) permission to “carve out.” This article discusses the labeling “carve out” battles waged before FDA over the last few years involving both patents and exclusivities, explains why the generics have been winning, and offers strategies for pioneers who are seeking ways to protect new investments made in their old drugs.

Patents and Drug Labels—the Pioneer Opening

Patents have long been the crown jewels of the pharmaceutical industry. They protect pioneer therapies from generic competition and underwrite the enormous investment required for new drug research and development. What makes drug patents so valuable, however, is the Orange Book (OB) patent listing scheme established by the Hatch-Waxman Act and the automatic injunctive effect that these patents have on generic entrants.

Under Hatch-Waxman, pioneer manufacturers are required to list in the OB all patents that claim the drug or method of using the drug for which the manufacturer is seeking approval. If a generic manufacturer seeks FDA approval for the same drug before all OB-listed patents have expired, it must serve notice on the pioneer that it is challenging these patents. The pioneer then has an opportunity to file an infringement suit which automatically delays FDA approval of the generic for up to 30 months. Through clever use (generics would say manipulation) of the OB listing process, pioneers found that they could delay generic entry for many years simply by filing follow-on patents for minor improvements or secondary features in their drugs—a process which became known as “ever-greening.”

Things changed dramatically in 2003, however, when FDA overhauled its OB listing procedures to eliminate “ever-greening” and make OB listing of patents a less powerful and versatile weapon against generic competition. Over the next five years, pioneers saw the drug competition pendulum swing decidedly in favor of the generic industry. Today, generic drugs account for over 60 percent of prescriptions written and over 20 percent of total drug sales. With an estimated $65 billion of drugs coming off patent protection in the next five years, generics stand ready to cash in on this bonanza.

Pioneers have battled back, developing new protectable uses for their drugs, with some taking an aggressive strategy aimed at discovering novel features or secondary conditions that appear on drug labels in the form of patent-protected language. Their goal is to force generic manufacturers into a corner: if the generic copies the pioneer label as generally required by FDA rules, it risks infringing, or inducing infringement of, the pioneer patents; but if the generic seeks FDA permission to “carve out” the patent-protected language to avoid infringement (allowed under certain limited conditions explained below), it limits its market, in theory, to the non-protected conditions or uses, that may only represent a small or declining share of the pioneer’s market.

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“Carve Outs” and Off Label Prescribing—the Generic Response

In a perfect world, a pioneer who researches and develops secondary drug features or new conditions of use would have sufficient time to recoup its investment before generics would be allowed to compete. This, after all, was one of the principle objectives of Hatch-Waxman. In most cases, the pioneer would be protected either by getting three years of labeling exclusivity for new uses or conditions that were based on clinical studies and/or by getting patent protection for any discoveries capable of being patented. A generic would still be allowed to compete for uses and conditions not protected by exclusivity or patent, provided it could show FDA that its drug was as safe and effective as the pioneer for all non-protected conditions of use. In theory, such partial competition by generics (often referred to as “skinny labeling”) would lower the drug costs for some patients while still protecting the pioneer’s investment, for a limited time, in new conditions and discoveries.

Not surprisingly, pioneers do not live in a perfect world. What the Hatch-Waxman framers may have failed to contemplate when they adopted the skinny labeling, or generic “carve out” rule, was the practice—rare back in 1984 but increasingly common today—of doctors prescribing drugs and pharmacists filling prescriptions for so-called “off label” uses and thus, making the generic label not so skinny after all. Although a drug may not lawfully be marketed for an “off label” use, nothing prevents doctors from prescribing such use. Indeed, many drugs on the market (pioneer and generic) derive a significant share of their revenues from the treatments or uses that have never been approved by FDA. Compounding the problem for pioneers is the AB rating that a “carved out” generic can obtain which permits pharmacists—and in some states actually requires them—to substitute the generic for the pioneer even if prescribed “off label.” FDA has repeatedly pointed out that it is powerless to do anything about these practices because they are governed by state law.

Pioneers are understandably concerned that the “carve out” rule, coupled with the practice of prescribing and substituting generic drugs “off label,” threatens their ability to recover the large investments needed to discover new uses or to improve the safety or efficacy profiles for old drugs. And the situation may be getting worse. In response to a growing chorus of consumer complaints that too many drugs were being approved by FDA with little or no understanding of their long term side effects, Congress, in 2007, gave FDA new powers to force pioneers to conduct post-approval clinical studies. But, if pioneers are required to undertake such studies with little assurance they will be able to recover the costs through new exclusivities or patent protection, it will mean less money available to pioneers for researching and developing new drugs. This is what many drug manufacturers and some regulators fear is now happening.

“Carve Out” Scorecard – Generics 8, Pioneers 1

So how serious is the generic “carve out” threat? Since 2002, there have been nine cases decided by FDA involving “skinny labeling,” and only once has FDA sided with the pioneer. The reason that pioneers keep losing these battles may have more to do with their not fully understanding FDAs safety and effectiveness calculus rather than with the “carve out” rules themselves.

FDA regulations generally require a generic drug label to be identical to the pioneer label with limited exception. One exception, set forth in 21 CFR 314.127(a)(7), is where aspects of the [pioneer] labeling are protected by patent or by exclusivity and such differences do not render [the generic drug] less safe or effective than the [pioneer] drug for all remaining non-protected conditions of use. This exception applies to patents listed in the OB as well as all pioneer exclusivities—five-year new chemical entity, three-year labeling, Orphan Drug and pediatric.

When evaluating a generic “carve out” request, therefore, the test applied by FDA is whether any of the protected language is needed to make the generic as safe and effective as the pioneer for any of the conditions of use that are on the generic’s label. As the case studies that follow will illustrate, the “carve out” exception has been allowed by FDA where a generic will be foreseeably prescribed for an “off label” use, even if such use is the first line therapy for the pioneer drug. It has also been allowed where a new dosing regimen or harmful side effects are discovered for a new patient population—i.e., one not previously targeted on the pioneer label. However, FDA will not allow the carving out of safety or efficacy information directed to “on label” patient populations unless such information already exists elsewhere on the pioneer label.
Case Studies 2002-2008

1. Foreseeable “off label” use.
   FDA has decided five cases, four in 2008, dealing with foreseeable
   “off label” use: 1) in the Rebetrol/ribavirin case (2004), Valeant asked
   FDA not to approve any abbreviated new drug applications (ANDAs)
   with labeling that omitted the use of ribavirin in combination with PEG-
   Intron to treat HPC, a condition protected both by exclusivity and
   patents; 2) in the Ethyl/amifostine case (2008), MedImmune requested
   FDA not to approve any ANDAs that
   omitted patent-protected dosage and
   administration information related to
   the treatment of head and neck cancer;
   3) in Marinol/dronabinol (2008), Solvay asked FDA not to approve
   any ANDAs with labeling omitting the treatment of anorexia in AIDS
   patients, a use protected by patent; 4) in Camptosar/irinotecan (2008),
   Watson, the first to file an ANDA, asked FDA not to approve any other
   ANDAs with labeling that omitted a
   combination use with other drugs to
   treat colon cancer which was the “first
   line therapy” for the pioneer drug; and
   5) in Prandin/repaglinide (2008),
   Novo Nordisk asked FDA not to
   approve any ANDA’s that omitted the
   use of repaglinide in combination with
   metformin, a use protected by patent.

   In each of these cases, FDA was
   willing to concede there was a strong
   likelihood the generic drug would be
   prescribed for the “carved out” use
   and, moreover, that such use would,
   in most cases, be unsafe without
   protected information on the label.
   Nonetheless, FDA ruled that it is
   bound by its regulations to look solely
   at the “non-protected conditions
   of use” when making its safety and
   effectiveness in comparison—meaning
   that any “off label” use of the generic
   would not, in and of itself, be relevant
   to such determination. Accordingly,
   in each case the generic drug with the
   omitted use was found by FDA to be
   no less safe or effective than the
   pioneer.¹⁴

2. New Dosing Regimen for New
   Patient Population.
   In the Ultram/tramadol case
   (2002), three generics asked FDA for
   permission to omit a patent-protected
   pain medication schedule from the
   pioneer (Johnson Pharmaceuticals)
   label. The protected labeling, added by
   supplement, was indicated for patients
   found to be intolerant of the drug
   when administered under the titration
   schedule recommended for rapid
   onset of the drug. The issue presented
   to FDA was whether a generic drug
   with the “carved out” titration schedule
   might result in higher discontinuations
   due to side effects. If so, the generic
   drug would be considered less effective
   than the pioneer, and the protected
   language could not be “carved out.”

   FDA examined the clinical studies
   supporting the lower titration schedule
   and found that they were conducted
   only on patients who had already
   discontinued the drug due to side
   effects. These patients, however,
   were considered to be a new patient
   population not specifically targeted on
   the original label. Thus, in evaluating
   the safety and effectiveness of a
   generic with the new patient dosing
   schedule omitted, FDA could only
   look to the results for the general
   patient population, not the new
   population, and determined the
   generic would be no less safe or
   effective than the pioneer for this
   group. Had the pioneer’s clinical
   study not been limited to users
   identified as intolerant to the drug,
   FDA indicated that the patent-
   protected language could not have
   been omitted from the label.

3. New Dosing or Safety Information
   for an Existing Patient Population.
   The Oxandrin/oxandrolone case
   (2006) involved a study performed by
   Savient on geriatric patients who
   needed to gain weight following
   surgery. The drug had been approved
   for weight gain by “adults” generally,
   and the new study sought to determine
   whether the geriatric sub-population
   required special dosing or warnings as
   to side effects. FDA granted three-year
   labeling exclusivity for certain geriatric
   data obtained from the clinical study
   and Savient asked FDA to prevent
   any generic from “carving out” the
   protected language.

   In performing its safety and efficacy
   analysis, FDA compared the protected
   geriatric information with all of the
   non-protected conditions on the
   pioneer label and found that such
   information was already “adequately
   addressed” elsewhere on the label.
   Specifically, FDA found that the new
   geriatric dosing regimen fell within
   the existing range recommended for
   adults generally, and the new geriatric
   side effects had also been previously
   identified on the label. As a result,
   FDA concluded that the protected
   geriatric language could be “carved
   out” without rendering the generic less
   safe or effective than the pioneer drug.

4. New indication “intertwined” with
   existing indication.
   The Altace/ramipril case (2008)
   dealt with a drug approved initially
   to treat hypertension that was later
   studied and approved for reduction in
   risk of myocardial infarction, stroke
or death in patients with certain types of cardiovascular disease. The pioneer, King Pharmaceuticals, asserted that these new “heart outcome” indications were “intertwined” with the hypertension indication and could not be removed from the label without compromising the safety or efficacy of the drug for hypertensive patients.

FDA reviewed the clinical data and found that while hypertensive patients made up almost half the study, the results were reflective of the “larger population” of patients at risk of myocardial disease. Thus, it could not be said that the new beneficial effects of the drug were connected to a reduction in blood pressure in the hypertensive patient population. Accordingly, FDA concluded that the new indications were not related to an increased efficacy in the existing hypertensive patient population and could be “carved out” without rendering a generic less safe or effective than the pioneer. Had the study found greater benefits in hypertensive patients, however, FDA indicated that such information could not have been omitted from generic labels.

5. New Use Involving Migrating Patient Population or Progressive Disease.

The Rapamune/sirolimus case (2004), involved a Wyeth drug that had been approved for use in combination with cyclosporine as an immunosuppressant for renal transplant patients. Due to a danger of renal impairment from long term use, Wyeth conducted a follow-on study on low to moderate risk (but not high risk) patients to determine whether a withdrawal regimen for cyclosporine might lead to safer use of the drug. Eventually, new safety data on cyclosporine withdrawal was added to the label, and FDA granted three years of pioneer labeling exclusivity.

Wyeth petitioned FDA not to approve any generic with the new safety data “carved out” on the grounds that this would render the generic less safe than the pioneer for all non-protected conditions of use. FDA reviewed the clinical data and agreed with Wyeth. It said that although the study was based on low to moderate risk patients, the new labeling contained “critical prescribing information” for all patient populations, including high risk. FDA reasoned that if the protected language were “carved out,” generics could only be safely and effectively be labeled for use by high risk transplant patients. But, it said, this could lead to confusion among drug users and potentially unsafe use if and when high risk patients “migrated” to medium or low risk for which the generic would not be properly labeled. Therefore, FDA refused to allow any generic “carve out” during the exclusivity period.

The Prandin/regaplinide case (2008), noted above, addressed the issue of a labeling “carve out” in the context of type 2 diabetes, a “progressive” disease. Prandin had been approved both as a monotherapy and in combination with metformin and/or thiazolidinediones (TZDs). Novo held a patent that protected the metformin combination until June 2018, and it petitioned FDA to refrain from approving any ANDAs with information on this combination therapy omitted from their label. Among other assertions, Novo contended that the omission of information on the co-administration of repaglinide and metformin would ignore the progressive nature of type 2 diabetes, misleading patients and doctors, and rendering any generic less safe and effective than Prandin.

The question presented to FDA was whether a disease that is known to be “progressive,” such that patients would be likely to progress over time from one treatment (e.g., monotherapy) to another (e.g., combination therapy), would require both indications on a generic label for the safe and effective use of the drug. In addressing this issue, FDA evaluated the clinical trial data described in the Prandin labeling and concluded that it contained no safety data from the Prandin/metformin clinical trial and that all safety information on the label would remain after “carve out.” Accordingly, it ruled that an omission of the metformin information would not render a generic less safe or effective than Prandin for the remaining uses.

**Skinny Labeling Simplified**

An examination of the nine cases decided since 2002 suggests that the FDA’s safety and efficacy analysis for “carve outs” can be deconstructed into the flow chart depicted in Figure 1. A pioneer drug manufacturer seeking to determine whether a generic might be allowed to “carve out” protected labeling for an existing or new use of its drug product, might then apply the following analysis:

Step 1—Identify the protectable labeling language. FDA ultimately will determine what language is protectable by exclusivity based on the clinical studies submitted. If the language is subject to patent protection, it will only be eligible for “carve out” if the patent is listed in the OB.

Step 2—Remove all of the protected language from the pioneer label. This becomes the non-protected conditions of use (NPCU) labeling to which the
comparative safety and efficacy analysis is then applied.

Step 3—Analyze and compare the protected language in Step 1 with the NPCU labeling in Step 2 to determine if the protected language provides any safety and efficacy information that is relevant to any conditions of use for any patient population on the NPCU label. Consideration should be given to progressive diseases and the likelihood of “migrating” patient populations.

Step 4—If the protected language is not needed for safe and effective use of the drug with the NPCU label, the “carve out” will be permitted.

Step 5—If the protected language is needed for the safe and effective use of the drug with the NPCU label, the “carve out” will not be allowed unless those safety and efficacy issues are adequately addressed elsewhere on the NPCU label.

Overlaying this theoretical model onto the “carve out” cases, some general principles start to emerge for evaluating whether a proposed clinical study might or might not lead to new uses that are protectable from future generic “carve outs.” For example:

- If the new condition of use (i.e., the protected labeling language) involves a new indication that is not “intertwined” with other indications on the NPCU label, generic “carve outs” will generally be allowed;
- If the new use involves dosing, administration, warnings, etc., for a new patient population (i.e., one not on the NPCU label), generic “carve outs” will generally be allowed;
- If the new condition of use relates to safety or efficacy for an existing (NPCU label) patient population, generic “carve outs” will generally not be allowed; and
- If the new condition of use relates to safety or efficacy for a new patient population that an existing (NPCU label) patient population is likely to become, generic “carve outs” will generally not be allowed.

**Labeling and Life-cycle Protection**

Exclusivity and patent protection are critical factors in the life-cycle planning of every successful drug. For pioneers to ensure they will be able to take full advantage of these well-earned protections, a firm understanding is required as to how the generic labeling “carve out” rules work and what pioneers can do to ensure these protections...
are not easily circumvented; moreover, as the foregoing case studies clearly illustrate, pioneers should be thinking about these issues long before generics are preparing to enter the market. Following are some key stages in the drug development life cycle where label protection strategies might be implemented to protect clinical investments.

1. Patent claims drafting

Discoveries made during preclinical and clinical investigations (including postapproval studies) can often lead to patentable features that appear on drug labels. Protected labeling language that comes from patents not listed in the OB cannot be “carved out” by generics and can present formidable barriers to generic entry. Examples of these might include methods of manufacturing, diagnostic screening and distribution or tracking patents.21

Patentable discoveries impacting safety or efficacy and drafted as method claims can appear on labels in the form of dosage/administration data, warnings, precautions, contraindications or adverse drug reactions.22 These types of patents must be listed in the OB and, theoretically, are eligible for “carve out.” How they appear on drug labels, however, will largely determine whether they can be omitted by generic drug manufacturers. As the case law now illustrates, patent claims that deal with safety and efficacy issues involving non-protected indications or patient populations are more likely to survive “carve out” attempts than those that do not.

An aggressive patent prosecution strategy focused on life-cycle protection should involve not only the careful “mining” of clinical data but also a closer working relationship with regulatory personnel involved with clinical study design. By coordinating these two critical functions, while keeping an eye on the label, pioneers will be better positioned to ensure that their drug protections are maximized and clinical investments protected.

2. Clinical Study Design

Clinical studies can have varying goals that are sometimes in conflict, for example, improving patient health versus drug profitability. No study, however, is designed to lose money for a pioneer. To this end, exclusivity and patent protections are important factors that need to be addressed in nearly every study.

The “carve out” cases teach some important lessons for clinical designers looking to protect drugs coming off exclusivity or patent protection or who are simply looking to regain a competitive edge over generic competition. Studies that are fashioned to add new indications will have a much greater chance of yielding protected labeling language that cannot be “carved out” if the indications are intertwined with existing treatments. Labeling omissions can also be thwarted if clinical studies are designed to add safety and efficacy information that address existing conditions of use or patient populations already targeted on the pioneer label. Studies that focus on new conditions of use for patient sub-populations are also more likely to generate labeling that cannot be “carved out” if the sub-populations are sufficiently large in comparison to the drug’s intended population, or if other sub-populations are likely to migrate into or out of the protected population.23

None of this is to suggest that clinical studies can be easily altered or designed to ensure that, if successful, they will necessarily lead to labeling protections immune to generic “carve out.” However, study developers who understand how the FDA labeling rules operate, who can anticipate how labeling protections tie in with the clinical studies and who are able to integrate their patent and regulatory functions to bring these protection about stand the best chance of recovering their research and development costs ahead of generic entry.

3. FDA Labeling Negotiations

Nothing is more troubling to a pioneer than discovering its hard-earned patent claims do not correspond with the labeling approved for the drug. A good example of this occurred in a recent litigation when a pioneer discovered that a miscommunication between its patent and regulatory departments resulted in the range of a key ingredient appearing on the drug label differently than claimed in the patent. This mix-up gave generics an opening to label their drug within the range of the pioneer label with no risk of infringement. Had the patent and regulatory departments been better coordinated, generic entry would have had to await patent expiration.

For protected language to be of any value, it must appear correctly on the pioneer label. This means that pioneer’s regulatory department needs to coordinate draft labeling language with its patent counterparts and possibly include them in negotiations with FDA staff during application review. Individuals charged with labeling responsibilities should have superior negotiating skills, a firm understanding of how pioneer labels can be changed (e.g., to add protected language) without requiring FDA approval, and a sense of how to ensure that generics on the market adhere to their own labeling responsibilities.
OB Filing Use Code Selection

As noted above, patents not listed in the OB cannot be “carved out” of a generic label. While this might look like an opportunity for pioneers to thwart generic entry by not listing eligible patents in the OB, they would be advised to approach such temptations with caution. Under FDA rules, patent declarations (including a declaration that no patent can be listed) must be filed under “penalty of perjury” with the initial NDA, each supplemental filing, and upon NDA approval.24 A false declaration not only could land a pioneer in trouble with FDA, but it might also raise an estoppel defense in a subsequent infringement litigation.

OB use code listings, however, appear to be more flexible. Every method of use patent listed in the OB is assigned a use code, selected by the pioneer, which is supposed to briefly describe the use claimed in the patent. Use codes are important because a generic that seeks to “carve out” a patented condition use from the pioneer label must “carve out” all uses which fit the description. Thus, for example, a listed patent that claims a specific combination drug use that is given a broad use code (e.g., “for use in combination with other drugs”) could force generics to “carve out” all combination therapies on the pioneer label regardless of whether all are protected.25 An examination of the current list of OB use codes reveals this to be an area over which FDA has exercised no oversight mainly because of its long-standing policy of not getting involved in reading patent claims.

Conclusion

Pioneers focused on protecting their investments in new uses for old drugs or improvements to the safety or efficacy profile for these drugs would be advised to study carefully the FDA “carve out” decisions to see what works and what doesn’t. One reason generics keep winning these battles is because pioneers have yet to figure out how to coordinate their patent and regulatory functions to maximize available protections. As pioneers learn to bridge this divide in the key stages of their drug development lifecycles—from claims drafting to clinical study design to labeling negotiations—they will stand a much better chance of recovering their investments by way of the exclusivities and patent protections they seek. △

4. The analysis herein deals with generic labeling “carve outs” generally, which can occur in one of four ways: (1) if the labeling is protected by exclusivity (e.g., three year data, orphan drug, etc.) the “carved out” language is identified in the generic FDA application; (2) if the labeling is protected by a method of use patent listed in the OB, the generic could file a “section viii” statement in lieu of a patent certification (see 21 C.F.R. 314.92(a)(1) and 314.94(a)(12)(ii)); (3) if the labeling is protected by a drug product patent listed in the OB (e.g., composition, formulation, etc.) the generic would file a Paragraph IV certification; or (4) if the exclusivity or listed patent protects the strength, dosage, route of administration or active ingredients the generic can file a suitably petition with the FDA requesting a change in the drug and/or labeling (see 21 C.F.R. 314.3).
6. As of this writing, there are pending Citizen Petitions involving generic labeling “carve outs” for Thalomid (thalidomide) and Actos (pioglitazone). In addition, in 2005, FDA asked for public comment on a patent “carve out” request by a generic involving Zithromax (azithromycin) which has yet to be resolved.
7. FDA’s general authority to permit generics to “carve out” pioneer labeling information has been recognized by various courts. See, e.g., Bristol-Myers Squibb Co. v. Shalala, 91 F.3d 1493 (DC Cir. 1996); Sigma-Tau Pharmaceuticals, Inc. v. Schwartz, 288 F.3d 141 (4th Cir. 2002).
8. FDA has interpreted the patent “carve out” regulation as applying only to OB-listed patents even though the legislation and its rules are silent on this requirement.
14. Although FDA expressed concern about the practice of “off label” prescribing, it noted that it had no authority over the practice of medicine or generic substitution by pharmacists, both of which are governed by state law.
15. In early 2008, FDA directed all oral anti-diabetic drug manufacturers to use a simplified indication on their label, thereby causing Novo to omit the specific indications for Prandin used as a monotherapy and in combination with metformin or TZDs. Other labeling sections, however, contained dosage and clinical information about metformin used in combination with Prandin and it was this information that was understood to be protected by the Novo patent.
16. FDA did not appear to address the efficacy issues in its “carve out” analysis.
17. In the Uluran case, FDA determined that certain information added to the pioneer label did not require clinical data for approval and, therefore, was not protected by three-year exclusivity.
18. Pioneers have been required to identify which method claims read on what parts of their drug labels as of the 2003 OB reforms. For patents listed in the OB before this date, FDA likely will accord pioneers considerable deference in determining what labeling language is covered by their patent claims.
19. A patient population (or sub-population) is “on” the NPCI label if it is explicitly or implicitly covered by the labeled treatment. For example, a geriatric population is a sub-population of adults but a pediatric population is not.
20. See Mahn, supra note 1, at 10.
21. A diagnostic screening patent might describe a particular screen carried out before a drug is prescribed or used to monitor a condition (e.g., a level of a metabolite or antibody in the blood while the drug is being administered). A method for distributing a toxic or addictive drug or tracking a vaccine might appear on the label if required by FDA rules or policies.
22. Two examples of issued patents with method claims similar to what would be required to claim drug warnings, precautions and adverse reactions are: U.S. Patent No. 6,683,102 and U.S. Patent No. 7,122,566. But see In re Biha, 545 F.3d 943 (Fed. Cir. (2008)) which limits patent eligibility of a process (e.g., the step of inquiring and advising of actions to be taken by a patient to avoid an adverse drug reaction) unless it is tied to a machine or apparatus, or transforms an article into a different state or thing.
23. Pediatric populations are subject to special rules re labeling “carve outs.” See FDAAA Title V, supra note 4.
24. FDA Forms 3542 and 3542a state that a knowingly false declaration of patent information is punishable under federal criminal statutes.
25. In one anecdotal case, FDA was asked by a generic to “split” a use code that covered three indications, only two of which were patent-protected. FDA indicated that it was bound by the pioneer use code and would not permit a carving out of less than all of the covered indications.