

co-trimoxazole, where sulfamethoxazole was combined with trimethoprim. More recent examples have focused on decongestants in combination with antihistamines, for example, loratidine and pseudoephedrine, antibiotic combinations such as amoxicillin and clavulanic acid, angiotensin-converting enzyme inhibitors in combination with diuretics such as enalapril and hydrochlorothiazide or perindopril and indapamide, and antihypertensives in combination with diuretics such as atenolol and chlorthalidone.

Use Patents

In certain instances, a drug substance has been found to be of benefit in treating disorders other than those first known and recognized, for example, with omeprazole with its relatively novel indication for use in gastroesophageal reflux disease and the amino-ketone antidepressant bupropion with the additional claim for use in smoking cessation. New clinical studies are undertaken to provide the additional “use” that permits the innovator company to claim that particular new indication on both label and package insert. “Use patents” prevent generic companies from making the additional claim(s) but do not prevent the generic product from being prescribed to treat conditions originally claimed in the basic patent. Consequently, “use patents” do not carry the same impact as process and formulation patents but nevertheless cannot be ignored.

LITERATURE SEARCH

A comprehensive literature search should be performed that focuses on the API material in question and the proposed formulation. The formulation patent(s) filed and information on the innovator’s New Drug Application can be obtained by requesting the Summary Basis of Approval from the FDA at <http://www.fda.gov/cder/foi/anda/index> and provides an excellent source of background information. It is essential that such a literature search be embarked upon as early in the development process as possible.

REGULATORY STRATEGY

Once all of the patents have been comprehensively analyzed, a regulatory strategy must be formulated to establish when the “earliest date of sale” of the generic drug product can legally be made. In this respect, the Approved Drug Products (Orange) Book [26] provides useful information relating to the expiration date of appropriate patents of drug products that are the subject of approved applications but exclude process patents. The reader is referred to Chapter 15 for a more comprehensive account. Such strategies need to embrace “first to file,” “exclusivity,” and a whole host of “legal implications” that need to be encompassed within the project plan, which will ultimately lead to a “first to market” strategy [27]. This scenario has evolved over the past 15 years and gained prominence for the first time when ranitidine (Form 1) Abbreviated New Drug Applications were reviewed by the FDA in the mid-1990s [28].

Once patent hurdles have been fully investigated, and regulatory strategies are put in place, it is up to the formulation scientist to ensure that a non-patent-infringing