PATENT RESTRICTIONS AND EXCLUSIVITY GRANTED TO AN NDA SPONSOR

The filing of an NDA with the FDA for a drug product made with an NCE results in the listing of "relevant" patents and periods of "exclusivity" for the approved drug product (frequently identified as the "listed drug"). This listing occurs in the FDA "Approved Drug Products with Therapeutic Equivalence Evaluations" and is referred to as the "Orange Book." The FDA now provides all of this information online at their website (http://www.fda.gov/cder). For an API supplier, the listed patents in the electronic Orange Book normally provide only those patents that protect the NCE (compound and method of use) as well as formulation patents (presumably those relevant to the filed drug product). Current issues concerning the listing of patents in the Orange Book are covered in Chapters 1 and 14 of this book. What is not a required listing in the Orange Book are process patents for the manufacture of the API or critical intermediates for the API, beyond the original patent(s) governing the NCE itself. This point is covered by a section of the Food Drug and Cosmetic Act, which authorizes an API supplier or an authorized party/agent for the API supplier to write to an NDA sponsor and request a listing of all relevant process patents that cover the filed NCE [6]. This is a fee for service request, with a maximum allowed charge of $500 for the service. The relevant U.S. Code information concerning patent infringements and penalties for infringement cited in Ref. [7] can be found at the website for the US Code.

With this list of process patents, the API supplier must now review all patents cited as well as conduct independent patent searches for all patents relevant to the NCE, which issued or were applied for in and outside the United States. This search should include not just the NDA sponsor but also any issued patent concerning the drug substance or any pivotal intermediate involved in the synthesis of the final drug substance. Specific aspects of the NCE that may be covered by process patents and other nonlisted patents in the Orange Book include particle size/surface area, morphic forms (polymorphs, hydrates, and solvates), and impurity/purity characteristics. The objective of the patent search is to determine what synthetic route to exploit for the manufacture of the target API, which will be noninfringing and cost effective and will yield finished API of appropriate quality and physical attributes suitable for formulation of the material into the targeted drug product for filing an ANDA.

Finally, with respect to "exclusivity" for the filing of an NDA, incorporating an NCE, the current regulations allow for a 5-year period of exclusivity before an ANDA can be filed incorporating the same API as the NCE. A different period of exclusivity is provided for the filing of formal supplements to NDAs, which is based on providing clinical data as part of the supplement. These points are covered in detail in Chapters 1 and 14 of this volume.

COMPARISON WITH INNOVATOR API

The challenge that the API supplier/manufacturer faces in entering the market place is to assure the user of the material that the API will be comparable with the innovator or pioneer drug substance, which is employed in an approved NDA drug product.