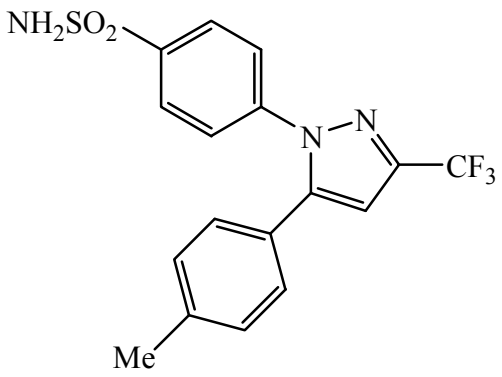
The celecoxib manufacturing process was redesigned with Green Chemistry objectives as part of the project's primary goals and resulted in dramatic environmental and worker safety improvements in the manufacture of the active ingredient in the medicine Celebrex®. While most submissions from the Pharmaceutical industry to the EPA Presidential Green Chemistry Award competition involve the significant redesign of the synthetic route, the simplicity of the celecoxib molecule precluded this approach. Thus, in order to make any significant improvement in the environmental burden in the production of celecoxib, a different approach was necessary. The only viable approach was to reduce the purification requirements by reducing the amount of the major impurities formed during the synthesis. A kinetic model for the formation of these impurities was therefore developed. During these studies, the elucidation of two unprecedented reaction mechanisms responsible for the formation of an isomeric impurity was identified. Application of this new mechanistic/kinetic understanding provided a significant increase in the process efficiency with respect to raw materials, solvents, energy and waste. For example, waste was reduced by 69 percent (greater than 5000 metric tons per year at current production levels.) The regulatory challenges of developing and implementing a pharmaceutical manufacturing process that isolates the final active pharmaceutical ingredient directly from a reaction mixture will be discussed.



Celecoxib