



ECR PHARMACEUTICALS

ECR PHARMACEUTICALS
P.O. BOX 71600
RICHMOND, VIRGINIA 23255
Tel: (804) 527-1950 Fax: (804) 527-1959

24 August, 2004

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 2004-N-0181

Dear Sir or Madam:

Please allow the following to comment on the FDA's recently established Critical Path Initiative

I am highly complimentary of this effort and trust that it will proceed on a reasonable time table toward development and implementation of its recommendations. An appropriate result of this initiative can provide a more efficient developmental pathway for both new molecular entities (NME's) as well as improved versions of currently marketed products. I offer the following comments for your consideration, with the notable focus on new dosage forms

Currently, only a few major firms have the technical and financial resources to develop or assume the development of NME's. The rest of the world shares the benefits of this development, but the citizens of the US assume the majority of the costs. The critical path initiative must assure that its recommendations facilitate and enhance US drug development and does not in any manner discourage it.

Smaller firms, as well as their larger counterparts, also have the capacity to develop improved dosage forms of currently marketed products which can enhance patient therapy. A more reasonable and less costly regulatory pathway to establish improved dosage forms of approved products would significantly encourage this development. Achieving lower developmental costs will result in a lower initial price of the product when approved. This pathway will also encourage more companies to develop products, will create more competition, and overall will result in improved products being available at lower costs. Having been in the industry for some 30 years, I am certain that regulatory requirements can be examined and revised to encourage economical drug development by more firms without sacrificing the essential assurances of efficacy and safety.

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As an overview, there are currently only three approval pathways available: 505(b)1 and 505(b)2 for NDA's and the ANDA process for generic drugs. The latter requires the newly developed drug be identical to the innovator or reference drug. The current ANDA format is fairly efficient in accomplishing the development of generic drugs and likely requires only minor modifications. The 505(b)1 is the path primarily used for NME's. While improvements can certainly be made to specific requirements, this path will not likely be significantly changed and will remain extremely expensive and out of reach of all but the larger pharmaceutical firms. The current 505(b)2 path which largely applies to enhanced dosage forms of drugs, modifies the 505(b)1 format. It allows for use of some phase 1 data, but thereafter is replete with redundant requirements and hence remains very expensive and generally out of the reach of smaller firms. Because 505(b)2 provisions provides for only three years of exclusivity, larger firms rarely take on this expense as the return will not be sufficient to sustain them. The economical development of new dosage forms of approved drugs requires substantial examination as such can make improved drug products available, stimulate competition, and lower drug costs.

Unfortunately the development of new dosage forms which can improve patient therapies, and accomplish the latter at a reasonable price, is not occurring with any regularity. A significant deterrent is not only the high costs related to the 505(b)2 requirements, but the 1959 regulatory provision which codifies that extended or modified release versions of approved, immediate release drugs are considered to be new drugs, hence requiring an NDA (and hence all of the provisions required of an NDA). This was sound reasoning in 1959 as extended release technology was somewhat new and unproven. Today, the technology is not only vastly improved, but is standard state of the art throughout the pharmaceutical industry. Additionally it is generally easily replicated and the release profile and bioequivalence of an extended release product can be readily demonstrated in pK studies. The cost of the latter assessment is generally reasonable, within the reach of small firms, and would also provide the necessary return to larger firms which may elect to dedicate resources to this type of development.

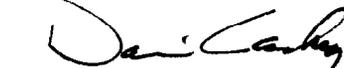
Because the modified release version of the approved drug requires an NDA, and two well controlled clinical studies as a part thereof, millions of dollars of costs are added to the project. This cost moves the project out of the reach of smaller firms, and makes is fiscally unacceptable to large firms. Additionally, at the end of the day, most would agree that the clinical studies contribute little to the body of knowledge about the drug, which is an already approved substance, and whose safety and efficacy are already confirmed as an immediate release entity.

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A refinement of the 505(b)2 path or the development of a similar new path which addresses and encourages the development of new dosage forms which utilize well established technology will improve patient therapy. Simplifying this process would encourage competition and result in these products being available at reasonable costs. And this can be accomplished without sacrificing assurances of efficacy and safety.

I would very much appreciate being included in future discussions as I believe I can provide appropriate recommendations, balance and insight. I will be happy to assume my own expenses as I believe this to be a very worthy and potentially productive undertaking which can benefit industry and patients, while allowing for the necessary oversight by FDA.

Best regards,



Davis S. Caskey
Vice President,
Pharmaceutical Operations
ECR Pharmaceuticals