WASHINGTON LEGAL FOUNDATION
2009 Massachusetts Avenue, N.W.
Washington, DC 20036
202 588-0302

September 20, 2006

By Facsimile [301-796-9877]
and First-Class Mail

Thomas Abrams, RPh, MBA
Director
Division of Drug Marketing, Advertising, and Communications
10903 New Hampshire Ave.
Bldg 22 Rm 1400
Silver Spring, MD 20903-0002

Re: NDA #21-416
Rythmol® SR (propafenone HCl) extended release Capsules
MACMIS ID #14383

Dear Mr. Abrams:

On September 14, 2006, the Division of Drug Marketing, Advertising, and Communications (DDMAC) sent a warning letter to Reliant Pharmaceuticals, Inc. (Reliant) alleging that two "promotional pieces" for Rythmol® SR (propafenone HCl) extended release Capsules misbranded the drug "in violation of" 21 U.S.C. § 352(a) and 321(n). The Washington Legal Foundation (WLF) requests that DDMAC immediately withdraw the warning letter for the reasons set forth below. We request, further, that DDMAC immediately begin a comprehensive review of its policies and procedures relating to prescription drug promotion to assure that they sufficiently respect the First Amendment and the statutory limitations on DDMAC's regulatory authority.

Inappropriate Regulation of Pharmacist-Directed Materials

It is not at all clear that DDMAC has the legal authority to regulate the content of communications not aimed at influencing prescribing decisions. The "promotional pieces" to which DDMAC objects in the warning letter are manifestly directed to pharmacists. The purpose of both documents is to alert pharmacists to the availability of a new 60-count bottle of Rythmol SR. According to Reliant, this bottle size is a "unit-of-use" package for Rythmol SR.

Traditionally, DDMAC has implemented the promotional labeling and advertising provisions of the Federal Food, Drug, and Cosmetic Act by focusing on detail aids, print advertisements, and

other promotional materials aimed at prescribers or (more recently) patients. These communications qualify as promotion because they recommend or suggest use of a product and propose that the prescriber order (or that the patient request an order of) the drug. It is inappropriate, we submit, for FDA to turn its attention to materials, like the brochure, that are aimed at completely different audiences, and that focus on the period after the prescribing decision has already been made. DDMAC's apparent determination that pharmacist-directed communications are subject to the same content regulation as conventional promotional labeling and advertising appears to represent a major change in policy. It reflects an impermissible and inadvisable extension of DDMAC's authority and should be abandoned.

DDMAC's regulation of these particular "promotional pieces" also appears to conflict with other established FDA policies. FDA increasingly has encouraged manufacturers to provide prescription drugs in so-called "unit-of-use" packaging to help address counterfeiting and to facilitate the distribution of Medication Guides to patients. Under the circumstances, it seems awkward, at best, for DDMAC to be objecting to Reliant's efforts to notify pharmacists about the availability of a new unit-of-use package for Rythmol SR.

This is not the first time that WLF has expressed this concern. On February 10, 2006, we requested that DDMAC withdraw an untitled letter that had been issued to Biogen Idec objecting to a communication aimed at facilitating reimbursement of the costs of a drug indicated in treating certain types of lymphoma. It is apparent from the warning letter to Reliant that DDMAC is continuing to push to or beyond the outer boundaries of its legal authority to reach heretofore unregulated categories of speech.

Omission of "Precise Approved Indication"

DDMAC contends that the "promotional pieces" "misbrand" Rythmol SR because they "fail[] to identify the limitations to its indication" and therefore imply—misleadingly, according to DDMAC—that the drug is useful in treating all atrial fibrillation patients. WLF would like to point out, as we have in numerous previous letters, that the very information that DDMAC claims is absent is actually present in the prescribing information accompanying the "promotional pieces."

It is not clear to WLF how including the approved indication for Rythmol SR in these materials would in any way advance the public health. The materials to which DDMAC objects are aimed at *pharmacists*. Pharmacists do not prescribe Rythmol SR. Whatever may be the case for promotional materials aimed at prescribers, it simply defies common sense that any decision to prescribe Rythmol SR would be influenced by revisions to materials aimed at pharmacists.

Double Disclosure Requirement

According to DDMAC, the "promotional pieces" are misleading because they "fail to provide" the risk information appearing in the FDA-approved labeling for Rythmol SR. In fact, all of this information appears in full FDA-approved prescribing information that accompanies the documents, as DDMAC concedes. Thus, pharmacists who receive the materials have immediate access to all of the information that DDMAC alleges is missing. Moreover, the information—

because it appears in the prescribing information—is presented in precisely the manner dictated by FDA. DDMAC's allegation that the "promotional pieces" are misleading because they omit this information is therefore factually untenable.

Nor does DDMAC have a credible legal or policy argument in support of its allegation. We have repeatedly explained some of the reasons that DDMAC's position is problematic. For example, it is unsupported by FDA regulations and inconsistent with FDA's established policy against overwarning.

WLF has repeatedly raised this issue with DDMAC in previous correspondence. We also provided a more extensive analysis of the issue in our August 7 report, which we have submitted to FDA in the form of a citizen petition. From the warning and untitled letters issued by DDMAC since WLF began its monitoring program, it is apparent that DDMAC has an established practice and policy of prohibiting manufacturers from disseminating promotional materials unless risk information appears twice—once in the "main body" or "creative" part, and again in the accompanying prescribing information or brief summary. Until DDMAC has provided a sufficient basis for this approach, no warning or untitled letters should be issued on the ground that a manufacturer has included insufficient risk information by failing to present that information in two places.

Lack of Authority to Compel Corrective Advertising

We have previously explained in detail the constitutional basis for our repeated request, which we make again here, that DDMAC discontinue its practice of demanding corrective promotion as a matter of course in all warning letters. Corrective promotion is not among the remedial actions expressly included among FDA's statutory authorities, and the courts have repeatedly found First Amendment violations in government demands that private firms engage in such advertising.

We believe, based on previous experience, that the "promotional pieces" at issue in DDMAC's warning letter to Reliant may have been disseminated many months ago. As you know, FDA regulations require manufacturers to submit specimens of their promotional pieces at the time of initial dissemination or publication, 21 C.F.R. § 314.81(b). It therefore seems reasonable to expect Reliant to have distributed the pieces at approximately the same time they were submitted to DDMAC. It typically takes DDMAC several months to issue a warning letter.

In light of these delays, corrective promotion is almost always inappropriate as a public health matter. WLF believes that any pharmacist who viewed the original pieces would only be confused if Reliant were to distribute "corrective" communications many months after the fact. To the extent pharmacists understand that the "corrective" messages relate back to another document that they might have seen months earlier, it is all too possible that communications intended by DDMAC to be remedial could end up simply confusing its intended audience. Given the warning letter's focus on the disclosure of risk information, these putatively corrective communications are virtually certain to emphasize the warnings associated with the product, thereby potentially misleading pharmacists into believing the drug is riskier than has been demonstrated.

Conclusion and Requested Action

For the reasons discussed above, we request that DDMAC immediately withdraw the warning letter to Reliant and cease the issuance of warning and untitled letters and advisory correspondence that contains allegations the same as or similar to those described above. We request that you review, in a systematic fashion, all of your policies and procedures to ensure that they provide sufficient room for manufacturers to disseminate, and health care practitioners and patients to receive, truthful and non-misleading information about prescription drugs. We request, further, that you respond to the numerous submissions that we have made to you since the DDMAC Watch program was initiated last year.

The deficiencies described in this letter do not necessarily constitute an exhaustive list. It is DDMAC's responsibility to ensure that its actions comply with the First Amendment, and do not exceed FDA's statutory authority.

Sincerely,

Richard A. Samp
Chief Counsel

cc: Sheldon Bradshaw (GCF-1)