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March 25, 2005

BY HAND DELIVERY

Division of Dockets Management
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

PETITION FOR STAY OF ACTION

Docket Nos. 2004P-0239 & 2004P-0523

The undersigned, on behalf of GlaxoSmithKline (GSK), submit this petition under 21 CFR 10.35 for a stay of *just three business days* -- beyond the point in time when GSK is first notified of FDA's decision to grant final approval -- of the effective date of any approvals FDA may decide to grant of abbreviated new drug applications (ANDAs) for generic versions of Flonase® (fluticasone propionate) or Beconase AQ® (beclomethasone dipropionate) Nasal Sprays.

The purpose of this petition is limited and the relief sought is narrowly drawn. GSK seeks the opportunity to initiate judicial review of any such approvals before generic products have entered the marketplace. A stay of action of three business days would allow GSK to seek temporary relief from a court with the *status quo* intact.

GSK is making this request in good faith, to avoid irreparable injury to its litigating and commercial position. The three day period being requested is *de minimis*, given that the underlying issues have been evolving for more than five years and that GSK's products have been "off-patent" for nearly one year, in the case of Flonase®, and more than ten years, in the case of Beconase AQ®. Sound public policy grounds support the entry of a brief administrative stay to allow GSK to consider and pursue its right to judicial review without being undermined by unnecessary shifts in underlying circumstances. For these reasons, and as discussed below, GSK is entitled to a stay of action under 21 CFR 10.35(e).

2004P-0239

PSA 1

A. DECISION INVOLVED

This petition for stay of action is being submitted in anticipation of possible approvals of pending ANDAs that reference GSK's pioneer nasal spray products, Flonase® and Beconase AQ®.

On May 19, 2004, GSK submitted a citizen petition requesting that FDA expeditiously issue a final guidance document setting forth a valid methodology for assessing the bioequivalence of nasal spray products, prior to approving ANDAs for generic versions of Flonase®. *See* Citizen Petition, Docket No. 2004P-0239/CP1 (Petition I).[1] GSK later supplemented this petition to include generic versions of Beconase AQ®. *See* Supplement to Citizen Petition, Docket No. 2004P-0239/SUP1 (Jan. 6, 2005). On November 23, 2004, GSK submitted a second citizen petition to ensure that generic versions of Flonase® meet the same high standard of quality that FDA has applied to GSK's product over the past five years, with specific reference to two *in-vitro* quality control specifications. *See* Citizen Petition, Docket No. 2004P-0523/CP1 (Petition II). Neither petition has been answered by the agency and no ANDAs have been approved to date.[2]

B. ACTION REQUESTED

GSK requests that the Commissioner of Food and Drugs grant a stay of *three business days* -- beyond the point in time when GSK is first notified of FDA's decision to grant final approval – of the effective date of any approvals FDA may decide to grant of ANDAs for generic versions of Flonase® or Beconase AQ® Nasal Spray.

C. STATEMENT OF GROUNDS

Under FDA regulations, the Commissioner of Food and Drugs is required to enter a stay in any proceeding where all of the following apply: (1) the petitioner will otherwise suffer irreparable injury; (2) the petitioner's case is not frivolous and is being pursued in good faith; (3) the petitioner has demonstrated sound public policy grounds supporting the stay; and (4) the delay resulting from

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[1] On November 15, 2004, the agency issued a letter stating that it had been unable to reach a decision on GSK's citizen petition because of the need to address other agency priorities. *See* Interim Response, Docket No. 2004P-0239/LET1.

[2] GSK has no information as to whether or when any such approvals will be issued or as to the ultimate disposition of the pending citizen petitions.

the stay is not outweighed by public health or other public interests. In addition, the Commissioner is permitted to grant a stay in any proceeding where it is in the public interest and in the interest of justice. *See* 21 CFR 10.35(e).

1. Irreparable Injury

Within days or even hours of the approval of ANDAs, generic versions of Flonase® or Beconase AQ® can be expected to enter the market. ANDAs will have been approved on the basis of "therapeutic equivalence" to Flonase® or Beconase AQ® and, as a result, generic substitution for GSK's products will readily take place. *See CollaGenex Pharms., Inc. v. Thompson*, Civ. A. No. 03-1405 (D.D.C. July 22, 2003) (describing the rapid erosion of sales that can occur when only a single generic product enters the market). Even if ANDA approvals are subsequently set aside, the monetary losses to GSK from improvident marketing could never be recouped, giving rise to irreparable injury. GSK has a right to seek equitable relief from a court to prevent such an irreparable injury without the *status quo* having been disrupted by premature generic entry.

The judicial standard for preliminary equitable relief requires that the moving party demonstrate not only that it will suffer irreparable injury, but also that an injunction will not substantially harm other interested persons. *See Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1066 (D.C. Cir. 1998). The greater the appearance of harm to other parties, the more difficult it will be for GSK to secure temporary or preliminary relief from a court. Allowing generic products onto the market, before GSK even has the opportunity to seek interim judicial relief, would significantly prejudice GSK: if generics have been able to enter the market, a reviewing court may view the balance of equities quite differently than had the *status quo* held.

2. Good Faith

GSK is pursuing this matter in good faith, and the issues at stake are serious and complex. Petition I joins important issues with which FDA has contended for years in a guidance development process seeking to establish a valid methodology for assessing the bioequivalence of nasal spray products. *See Draft Guidance for Industry: Bioavailability and Bioequivalence Studies for Nasal Aerosols and Nasal Sprays for Local Action* (June 1999); 64 FR 33869 (June 24, 1999). FDA initiated the guidance development process as far back as 1999.

GSK has submitted detailed comments on FDA's draft guidance documents and has participated in several scientific meetings on the subject. *See id.* at 5-6 n.5 & 7. GSK submitted Petition I only when it became apparent that some

ANDA sponsors petitioned FDA to grant approval from the agency without the guidance development process necessarily being completed. *See id.* at 2. Petition I raises a good faith question regarding FDA's ability to objectively determine the equivalence of nasal suspension products without first completing that process, and giving a reasoned response to scientific questions that remain pending.

Petition II builds on GSK's implementation, at the agency's urging, of an extensive research and development program to better ensure the quality of Flonase® with respect to two key device performance parameters, droplet size distribution and spray pattern. The purpose of Petition II is to ensure that the same standard of quality is applied in the same manner to all proposed generic versions of Flonase®. GSK's request for like treatment of like products is a good faith attempt to ensure parity within the marketplace for fluticasone propionate nasal spray products.

Both petitions raise good faith scientific and legal issues about a class of drug products – namely, nasal suspension products – that have confounded the agency and the industry for many years. In no sense are the issues "frivolous," and in no sense is GSK raising these issues without due cause. 21 CFR 10.35(e)(1).

3. Public Policy

The approval of any ANDAs for generic versions of Flonase® or Beconase AQ® can be expected to result in the rapid entry of those generic products into the stream of commerce. Reviewing courts are usually loathe to force affirmative changes in the *status quo*, pending full adjudication: if preliminary relief is granted at all, it more typically takes the form of an order that merely preserves the *status quo*. However, absent the requested stay of action, GSK will be forced to ask a reviewing court to do the extraordinary: pull the generic products back from the marketplace. A court may understandably be reluctant to go that far, particularly given the significance of the "balance of harms" factor in the preliminary relief analysis.

Sound public policy dictates that GSK's effort to seek equitable relief from a court not be compromised by unnecessary shifts in the balance of equities. There is no reason to allow the *status quo* to slip to GSK's detriment. A brief three business day stay to prevent a compound harm from unfolding, while GSK pursues judicial review as warranted, is wholly consistent with public policy.

4. Public Interest

The agency has been attempting to articulate a valid methodology for assessing the bioequivalence of nasal spray products, and has requested and overseen the implementation of tighter manufacturing specifications for Flonase®, for over five years. The ANDAs at issue in this case have themselves been under review by FDA for approximately two years. *See* Ivax Corp. Press Release (Mar. 7, 2003) at www.ivax.com. As well, the last-expiring patent barring the approval of generic versions of either Flonase® or Beconase AQ® expired more than ten months ago (taking into account the period of pediatric exclusivity). In this light, the brief stay requested – which is designed solely to preserve GSK's right to meaningful judicial review – is not outweighed by the public health or other public interests.

Moreover, "there is a strong public interest in meticulous compliance with law by public officials." *Fund for Animals v. Espy*, 814 F. Supp. 142, 152 (D.D.C. 1993). For example, the D.C. Circuit affirmed a decision that the public interest favored a preliminary injunction where "the public's interest in the 'faithful application of the laws' outweighed its interest in immediate access to [a] generic product." *Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1066 (D.C. Cir. 1998).

The *Mova* Court also specifically rejected the argument that the public's interest in the availability of generic drugs outweighs its interest in the faithful application of the laws:

> Both the FDA and Mylan also contend that the district court should have declined to issue a preliminary injunction in order to further the public's interest in the rapid movement of generic drugs into the marketplace. Supposing that they are right in their assessment of the public's interest, however, this factor alone cannot support denying an injunction. Our polity would be very different indeed if the courts could decline to enforce clear laws merely because they thought them contrary to the public interest; we decline to embark upon that path.

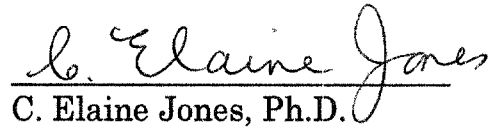
Id. at 1067 n.6.

The D.C. Circuit's conclusion is equally applicable in this case. The public has a substantial interest in ensuring the legal and scientific integrity of any approvals of generic versions of Flonase® and Beconase AQ®.

D. CONCLUSION

For the foregoing reasons, FDA should grant the requested stay. If the agency will not grant a mandatory stay, it should grant a permissive stay in the public interest and in the interest of justice. *See* 21 CFR 10.35(e).

Respectfully submitted,



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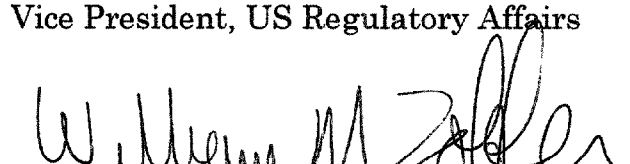

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