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Dockets Management Branch (HFA-305)
U.S. Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20857

Re: CP 03P-0160: Loratadine Tablets, 10 mg.:
L. Perrigo Company; Petition for Rejection of Section 505(b)(2) NDA

CITIZEN PETITION

On behalf of Novartis Consumer Health, Inc. ("NCH"), which markets loratadine tablets, 10 mg. ("Loratadine"), under an approved abbreviated new drug application ("ANDA") (ANDA 75-209), the following comments are hereby submitted to the Citizen Petition (CP 03P-0160) which was filed on behalf of Genpharm Inc. ("Genpharm") requesting that the U.S. Food and Drug Administration ("FDA") send a prompt letter ruling to L. Perrigo Company ("Perrigo"), refusing to approve Perrigo's pending 505(b)(2) application ("505(b)(2) NDA") for Loratadine. In connection herewith, reference is also made to the comments of Perrigo to CP 03P-0160, which were submitted by letter dated April 29, 2003 ("Perrigo's response").

For the reasons stated below, NCH agrees with the comments of Genpharm and the action requested in its petition and disagrees with the comments of Perrigo.

Rather than re-state the well-reasoned arguments expressed in the Genpharm petition, this letter will focus on two issues, which were implicitly raised in Perrigo's response:

- Assume that (i) at the time of submission of a registration application, the applicant technically meets the requirements for filing a 505(b)(2) NDA but (ii) prior to approval of the application, the conditions for filing a 505(b)(2) NDA are no longer met and the appropriate type of application is an ANDA. Under those circumstances, should FDA refuse to approve the 505(b)(2) NDA? NCH believes that the answer to that question is Yes.

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- Notwithstanding the foregoing, do equitable considerations exist which may justify approving the application as a 505(b)(2) NDA and do any of those circumstances apply to Perrigo's application? NCH agrees that there may circumstances in which it would be appropriate to "grandfather" a pending 505(b)(2) application but believes none of those circumstances exist with Perrigo.

1. **FDA should refuse to approve a 505(b)(2) NDA when the conditions for filing the 505(b)(2) NDA are no longer met and the appropriate type of application is an ANDA.**

As FDA made clear in its 1999 draft guidance document entitled *Guidance for Industry: Applications covered by Section 505(b)(2)* (the "Guidance"), ANDAs and 505(b)(2) NDAs are different types of applications serving different purposes and having different criteria for eligibility. Thus, they are not substitutable for each other and an applicant cannot, as Perrigo has done, pick and choose which application to use in order to avoid the statutory and regulatory restrictions that may apply to the other application.

An ANDA is the appropriate application for a drug which is the same as or "identical" to an already-approved drug. As stated in the Guidance, a drug is considered the same as, or "identical" to, an already-approved drug if it is identical in, among other things, active ingredient, dosage form, strength, route of administration, labeling, quality, performance characteristics, and intended use (see, also, 21 C.F.R. §314.92(a)(1)).

A drug should only be registered under a 505(b)(2) NDA when it is not "identical", as defined above, to the reference listed drug, meaning that the drug covered by the 505(b)(2) NDA has not been determined to be safe and effective for use under the conditions prescribed, recommended or suggested in the labeling thereof (see the definition of "new drug" under 35 U.S.C. § 201(p)). In other words, as explained in the Guidance, a 505(b)(2) NDA should only be used where the registrant is seeking approval of a change to an approved drug that may not be submitted under an ANDA because approval will require the review of clinical data. A 505(b)(2) NDA is not the appropriate application for duplicates of approved products that are eligible for approval under an ANDA.

Left unanswered by the Guidance and FDA's regulations is what happens if, after a 505(b)(2) NDA is filed but prior to approval, the requirements for filing a 505(b)(2) NDA are no longer met because the proposed drug is deemed fully "identical" to the listed drug and thus registrable under an ANDA. In the absence of the equitable considerations described below, NCH believes that there is no legitimate purpose to be served by allowing the registrant to maintain the 505(b)(2) NDA and that FDA should refuse to approve the 505(b)(2) NDA. To allow the registration as a 505(b)(2) NDA would ignore the different purposes behind the two types of applications as established by Congress and as recognized by FDA in the Guidance and in its regulations.

NCH strongly disagrees with Perrigo's argument that eligibility for filing a 505(b)(2) NDA should be determined solely at the time of the initial submission of the application; according to

Perrigo, subsequent changes in circumstances are irrelevant (see the Perrigo response). This mechanistic approach advocated by Perrigo would not only elevate form over substance but it would lead to absurd results.

The Perrigo situation is a perfect case in point. Perrigo's filing strategy is already described in detail in Genpharm's petition but it is instructive to repeat a few salient facts: Perrigo initially filed an ANDA (ANDA 76-301) for Loratadine on February 22, 2002. Perrigo, along with every other Loratadine applicant, recognized that Loratadine would soon be approved for the over-the-counter ("OTC") market. Schering Corporation ("Schering"), manufacturer of Claritin®, announced in March 2002 that it would seek OTC status for the drug and an FDA advisory panel had recommended a year earlier that FDA approve such a switch. Sensing an opportunity to catapult its application over the multiple other generic applicants and to avoid NCH's exclusive marketing rights under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act ("Hatch-Waxman"), Perrigo repackaged its application as a 505(b)(2) NDA and, on or about November 1, 2002, submitted it to the FDA.

The Perrigo product covered by its 505(b)(2) NDA was, in every respect, identical not only to the product covered by its original ANDA but also to Schering's Claritin®, except that the OTC switch of Claritin® had not yet been formally approved by the FDA. Along with every other Loratadine applicant, however, Perrigo understood that the OTC switch was just a matter of time and would likely occur on or before December 19, 2002, the expiration date of Schering's pediatric exclusivity which attached to U.S. Patent No. 4,282,233. In fact, FDA approved Schering's supplemental NDA for the OTC switch in November 2002, at most several weeks after Perrigo submitted its 505(b)(2) NDA.

According to Perrigo, all of the foregoing is meaningless because the only relevant question is whether its 505(b)(2) NDA met the technical requirements for filing eligibility at the time of submission. Taking this argument to its extreme (which, in fact, is very close to the Perrigo situation) would result in the following: Assume that (i) the FDA approved Schering's supplemental NDA on November 2, 2002; (ii) a generic applicant submitted a 505(b)(2) NDA for an OTC Loratadine on November 1, 2002, seeking to rely on FDA's previous findings of safety and efficacy for Claritin®; and that, two days later, on November 3, 2002, a second generic applicant submitted an identical 505(b)(2) NDA for an OTC Loratadine, also seeking to rely on FDA's previous findings of safety and efficacy for Claritin®. Under Perrigo's interpretation, FDA should approve the first application as a 505(b)(2) NDA but refuse to approve the second application.

The foregoing, NCH submits, makes no sense. Both applications should, as should Perrigo's, be denied approval.

2. **Even if equitable considerations may exist which would justify approving an application as a 505(b)(2) NDA when the eligibility requirements are no longer satisfied, none of those circumstances apply to Perrigo's application.**

NCH can conceive of circumstances in which it may be appropriate to allow a registrant to continue to maintain its application as a 505(b)(2) NDA even though the eligibility requirements are no longer met. By analogy to the FDA's decision to apply prospectively its change in the definition of triggering "court" decision for purposes of determining the start of the 180-day exclusivity period and the termination of the 30-month stay under Hatch-Waxman, it may not be reasonable, in a particular instance, to refuse to approve a 505(b)(2) NDA if that would be manifestly unjust or would unfairly penalize the applicant. (See FDA's March 2000 Guidance entitled *Court Decisions, ANDA Approvals, and 180-Day Exclusivity under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act.*)

In the case of an OTC switch, for example, equitable considerations might prevail if the applicant filed its 505(b)(2) NDA long before the OTC switch is approved and while the safety and efficacy of an OTC version of the listed drug is still being debated and the outcome of that debate remains uncertain. In this regard, it would be especially relevant if the applicant conducts, and submits with its 505(b)(2) NDA, studies necessary to establish the safety and efficacy of its drug for the OTC market.

NCH, however, can conceive of no injustice that would result from refusing to approve Perrigo's 505(b)(2) NDA. It filed its application at a time when it knew that the OTC switch of Claritin® was imminent. Indeed, based on that knowledge, it had previously filed an ANDA just like the other Loratadine applicants. In addition, Perrigo's response made no mention of having conducted any safety or efficacy studies for an OTC Loratadine. Instead, every indication is that Perrigo simply tried to take advantage of a window of opportunity by repackaging, without more, its existing ANDA for Loratadine as a 505(b)(2) NDA. A clever strategy but poor justification for approving the 505(b)(2) NDA.

If anyone has a right to claim injustice it is NCH. Perrigo is well aware that NCH is currently marketing OTC Loratadine under the Hatch-Waxman 180-day exclusivity period which was awarded to its affiliate, Geneva Pharmaceuticals, Inc. ("Geneva"). Perrigo is also aware that 505(b)(2) applications are not subject to an ANDA holder's claims to 180-day exclusivity. There is no doubt that a key objective of Perrigo's strategy is to by-pass NCH's exclusive marketing period, an extremely valuable right which Geneva earned through years of hard-fought and expensive litigation with Schering. If Perrigo is allowed to market it product under its 505(b)(2) NDA prior to the expiration of the 180-day exclusivity period, the loss to NCH and to Geneva could be significant.

For all the reasons set forth above, FDA should refuse to approve Perrigo's 505(b)(2) NDA.

Respectfully submitted,

David Tolman