

November 1, 2004

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

**RE: Docket No. 2004P-0386**

Dear Sir or Madam:

On September 24, 2004, Reliant Pharmaceuticals, Inc. submitted a comment on this petition ("Reliant Comment"). The Reliant Comment fails to provide any legally sound justification for FDA to deny the petition filed by Abbott Laboratories ("Abbott") and Laboratoires Fournier SA ("Fournier"). From the plain meaning of the relevant statute and a reasoned opinion from a Federal District Court, it is clear that a 505(b)(2) applicant relying on the investigations that formed the basis for approval of the fenofibrate formulation covered by NDA 21-203 must certify to the patents listed for NDA 21-203.

**I. RELIANT MISREADS SECTION 505(b)(2)(A).**

Reliant asserts that it "properly certified to the only patent which claims the drug for which and on which the investigations on which Reliant relies were conducted – the '726 patent." Reliant Comment at 3 (emphasis in original).<sup>1</sup> The statute, however does not limit the certification requirement to patents claiming drugs "for which and on which" the investigations relied on were conducted. Rather, it requires a certification "with respect to each patent which claims the drug for which such investigations were conducted . . .," FDCA § 505(b)(2)(A) (emphasis added).

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<sup>1</sup> Reliant's assertion is factually inaccurate. The '726 patent did not claim either the active ingredient (fenofibrate) on which animal safety tests were performed or the original capsule formulation on which the clinical trials were performed. Instead, it claimed the formulation of the marketed capsule. Thus, the '726 patent bears the same relation to the articles on which the investigations were conducted as do the four patents (the '670, '405, '552, and '881 patents) as to which Reliant has refused to certify.

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“For which” does not mean the same thing as “for which and on which.” The word “for” implies a future goal or object. A standard dictionary defines “for” as follows:

- 2 a:** as a preparation toward (dressing ~ dinner) or against (storing nuts ~ the winter) or in view of (making plans ~ retirement) (studying ~ examinations): having as goal or object (volunteered ~ the air force)
- b:** in order to be, become, or serve as (originally built ~ a church) (ordered eggs ~ breakfast)
- c:** in order to bring about or further (working ~ the good of humanity)
- d:** to supply the need of (food ~ hungry mouths)

*Webster's Third New International Dictionary of the English Language Unabridged* 886 (1964) (Tab 12). In contrast, the word “on” does not imply a future goal or object. Compare *id.* (definition of “for”) (Tab 12) with *id.* 1574-75 (definition of “on”) (Tab 13). In section 505(b)(2)(A), Congress could have used the word “on” or the expression “for and on,” but it did not; instead, it used the word “for.” FDA (and the courts) must respect that congressional choice.

In using the phrase “for which such investigation were conducted,” Congress meant what it said – that a Section 505(b)(2) applicant must certify with respect to each patent claiming the drug for which such investigations were conducted. This includes formulations that were a goal, object, or purpose of the investigations – in other words, future drug products developed by or for the sponsor of the investigations (or a party with a right of reference or use from the sponsor), and it is not limited in the manner suggested by Reliant. As the court stated in *Marion Merrell Dow, Inc. v. Hoechst-Roussel Pharmaceuticals, Inc.*, No. 93-5074 (AUT), 1994 WL 424207 (D.N.J. May 5, 1994) (“*MMD*”), “[a] certification must include any patent which covers *a drug for which the investigations were conducted.*” *MMD*, p. 3 n. 2 (italics in original).<sup>2</sup>

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<sup>2</sup> Contrary to Reliant’s assertion, Reliant Comment at 6, the expression “the drug for which such investigations were conducted” would not include a drug covered by an unrelated generic application because, in the absence of a right of reference or use, it cannot properly be said that the sponsor’s investigations were conducted “for” the generic applicant’s drug. Future approval of such a drug was not a goal, or object, or purpose of the investigations.

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Reliant attempts to excuse its failure to meet the statutory mandate by asserting that FDA's regulations change the statutory certification requirement by equating "drug for which" with "drug on which." This is not, and could not be, correct. FDA has never taken the position that a 505(b)(2) applicant relying on studies used to approve multiple NDAs is required to certify only as to patents covering the substances or compounds on which, as opposed to for which, investigations were conducted or sponsored. Instead, FDA and applicants have treated section 314.50(i)(1)(i)(A), appropriately, as a paraphrase of the statute, intended to have precisely the same meaning as the statute.<sup>3</sup> If and to the extent that FDA's regulation, 21 C.F.R. § 314.50(i)(1)(i)(A) (2004), were interpreted as changing the patent certification requirement from that prescribed by the statute, the regulation would, of course, be invalid as contrary to the statute.

## **II. RELIANT'S ATTEMPT TO DENIGRATE AND DISTINGUISH THE MARION MERRILL DOW DECISION FAILS.**

As Reliant now concedes, the only judicial decision addressing this issue – *MMD* – adopted the interpretation that the petition advocates. Rather than follow *MMD*'s reasoning, however, Reliant relegates its discussion of *MMD* to a footnote on the last full page of its Comment, and then tries unsuccessfully to denigrate and distinguish that decision.<sup>4</sup> Reliant Comment at 11 n. 9. The attempt fails.

Although Reliant seeks to dismiss the *MMD* decision, that case provided a well-reasoned analysis of the issue presented here. *MMD*'s reasoning has never been criticized, or even questioned, in more than a decade since *MMD* was decided. Although FDA's final rule promulgating section 314.50(i)(1)(i)(A) had not been published when *MMD* was decided, FDA had promulgated its proposed section 314.50(i)(1)(i)(A), which, like the final rule, used "on" rather than "for." Neither the preamble to the proposed rule nor the preamble to the final rule suggested in any way that FDA had made a conscious decision to change the statutory certification requirement as interpreted by the *MMD* court.

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<sup>3</sup> Reliant accuses Abbott of "completely ignore[ing]" the Letter from Janet Woodcock to Katherine M. Sanzo, Esq., Jeffrey B. Chasnow, Esq., Stephan E. Lawton, Esq., & William R. Rakoczy, Esq., Dkt Nos. 2001P-0323/CP1 & C5, 2002P-0447/CP1, & 2003P-0408/CP1 (Oct. 14, 2003). Opp. 5. In fact, although that consolidated response discusses certain other aspects of Section 505(b)(2), it does not discuss at all the scope of that provision's patent-certification requirement, and so does not bear on the issue here.

<sup>4</sup> See Tab 9 to the original petition.

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Reliant's attempt to distinguish *MMD* also fails. Reliant contends that Hoechst-Roussel ("H-R") merely "cited the wrong reference drug," and that here there can be no claim that Reliant has made such a mistake. Reliant Comment at 11 n. 9. The alleged mistake, however, was irrelevant to the decision.

The court's analysis rested on three propositions: (i) "[t]he section under scrutiny here modifies the word 'drug' by 'for which the investigations were conducted,'" *MMD* at \*3; (ii) "the drug for which the investigations were conducted was diltiazem and not immediate release diltiazem," *id.*; and (iii) "[a] certification must include any patent which covers a drug for which the investigations were conducted," *id.* n. 2 (emphasis added). The two patents at issue there (the '240 and '776 patents) covered sustained-release versions of diltiazem. *Id.* at \*1. Under the three-part analysis, the court held that H-R was required to certify as to those patents because they covered a Marion Merrill Dow ("MMD") diltiazem product. The fact that H-R's diltiazem product had the same dosage form as one of MMD's diltiazem products played no role in the court's analysis or its conclusion. The court's analysis and conclusion are indistinguishable from the instant situation.

### **III. RELIANT'S RELIANCE ON THE APPROVAL OF TEVA'S ANDA IS MISPLACED.**

Reliant overlooks key differences between the statutory certification requirements for ANDAs and for 505(b)(2) applications when it invokes FDA's approval of an ANDA submitted by Teva Pharmaceuticals USA for fenofibrate capsules that certified only as to the '726 patent. Reliant Comment at 9. Unlike Teva, Reliant is not an ANDA applicant, and approval of Teva's ANDA is irrelevant. Although the "requirements with respect to patent certification, notification of such certification to the patent owner, and exclusivity . . . are generally the same" for ANDAs and Section 505(b)(2) applications, 54 Fed. Reg. 28,872, 28,875 (July 10, 1989) (emphasis added)<sup>5</sup>, they are not the same (and FDA has never suggested that they are the same) in all material respects. Indeed, they differ in exactly the respect at issue here.

An ANDA is required to contain "a certification . . . with respect to each patent which claims the listed drug referred to . . ." FDCA § 505(j)(2)(A)(vii) (emphasis added). A Section 505(b)(2) application, on the other hand, is required to contain "a

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<sup>5</sup> The aspects of the two sets of requirements that are the same include: the four possible types of certification, the notice requirement in the case of a paragraph iv certification, the 45-day period for the filing of infringement litigation, and the provisions for when an approval may become effective.

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certification . . . with respect to each patent which claims the drug for which such investigations were conducted . . . .” FDCA § 505(b)(2)(A). The language of Section 505(b)(2)(A) plainly is broader. It is not limited to patents on a specific listed drug, but, as held in *MMD*, extends to the patents on each drug “for which such investigations were conducted.”

Therefore, approval of an ANDA subject to the different certification requirement of Section 505(j)(2)(A)(vii) has no bearing on the issue here, which depends on the interpretation of the broader and different language of Section 505(b)(2)(A).

#### **IV. RELIANT’S COMPLAINT ABOUT “EVERGREENING” HAS NO MERIT.**

Reliant’s argument about “perpetual evergreening,” Reliant Comment at 11-12, has no merit. What Reliant imagines is a perpetual series of new formulations covered by new formulation patents, to which a Section 505(b)(2) applicant would have to certify, and which might keep the applicant off the market forever. Reliant’s fears are ill-founded.

First, a patent on a new formulation would be subject to certification only if the innovator obtained approval of that formulation. FDA “interpret[s] the statute to permit listing of only those patents claiming the approved drug product and its approved uses.” 68 Fed. Reg. 36,676, 36,687 (June 18, 2003). “The drug product (formulation or composition) patents submitted must claim the specific drug product described in the pending or approved NDA.” *Id.* at 36,697.<sup>6</sup> *See id.* at 36,704 (amended 21 C.F.R. § 314.53(b): “For patents that claim a drug product, the applicant shall submit information only on those patents that claim a drug product, as is defined in § 314.3, that is described in the pending or approved application.”). Therefore, to support the listing of a formulation patent, an NDA-sponsor would need to develop a data package adequate to support approval of the formulation; and a patent on an unapproved formulation (or on any other unapproved aspect of a drug product) could not be listed, and so could not be the subject of a certification.

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<sup>6</sup> Even though patent information is submitted in newly filed and pending (*i.e.*, unapproved) NDAs, actual listing of a patent occurs only after approval of an NDA; and only patents covering an approved product will be listed. *See* 68 Fed. Reg. at 36,687 (“Although section 505(b)(1) of the act requires submission of patent information upon the filing of an NDA, we will rely only on the declaration form filed upon or after NDA approval under § 314.53(c)(2)(ii) to list patent information in the Orange Book.”).

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Second, the certification requirement would delay approval only if an applicant were sued for infringing a patent. A Section 505(b)(2) applicant would not infringe an endless series of formulation (or other) patents. The applicant would file certifications under Section 505(b)(2)(A)(iv) ("paragraph iv" certifications) to the inapplicable formulation (or other) patents, demonstrate non-infringement in its notification to the patent-holder, and very probably not be sued.<sup>7</sup>

Third, even if litigation did result from a paragraph iv certification, there would be no evergreening from a series of thirty-month stays. Under Section 505(c)(3)(C), as amended by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, a Section 505(b)(2) application will not be subjected to a thirty-month stay for any patent for which information is filed after the 505(b)(2) application is submitted, Pub. L. No. 108-173, § 1101(b)(2)(B) (2003) (amending FDCA § 505(c)(3)(C)).

Fourth, the availability of the narrower certification requirement of Section 505(j)(2)(A)(vii) provides an alternative pathway to the market for generic applicants. The interpretation of Section 505(b)(2)(A) presented here (and adopted in *MMD*) does not protect a patent-holder against competition from generic applicants under Section 505(j), the principal pathway for generic competitors. Rather, that interpretation merely preserves the particular balance between rewarding innovation and fostering competition that Congress intended when it adopted the broader certification requirement in Section 505(b)(2)(A).

In short, there is no basis under the statute or in reality for Reliant's contention that the petition's interpretation of Section 505(b)(2)(A) would lead to perpetual obstruction of the Section 505(b)(2) pathway to the market.

## **V. RELIANT'S INTERPRETATION OF SECTION 505(b)(2) WOULD LEAD TO ANOMALOUS RESULTS.**

In Reliant's view, the certification requirement for Section 505(b)(2) applicants would be limited to patents covering the specific formulation on which the investigations relied on were conducted. Under that approach, whether a 505(b)(2) applicant needs to certify as to a particular patent would depend entirely on whether the FDA requires that a

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<sup>7</sup> The instant situation illustrates the point nicely. Reliant filed a paragraph iv certification to the '726 patent, sent its notification, and was not sued. Had Abbott submitted to FDA information on many more formulation patents that Reliant clearly did not infringe, Reliant could similarly have filed paragraph iv certifications and there would have been no infringement litigation and no 30-month stay.

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new NDA or a supplement be submitted to support approval of the formulation covered by that patent.

Reliant asserts that “it is this product – the [non-micronized] 100 mg capsules approved under NDA 19-304 – ‘for which’ and ‘on which’ the studies were performed. . . .” Reliant comment at 8.<sup>8</sup> While Reliant states that “[t]he ’726 patent [as to which Reliant certified] is the only patent which claims the drug for which and on which the investigations on which Reliant relies were conducted” id. (emphasis in original), no one has ever contended that the ’726 patent claims the non-micronized 100 mg capsules. Instead, it is clear that Reliant certified as to the ’726 patent because it was listed for the 19-304 NDA, which covered both the non-micronized and, after approval of an NDA supplement, micronized capsule products.

The micronized capsule was approved under a supplement to the same NDA as the original non-micronized capsule, but could have been (as was the fenofibrate tablet product) approved under a separate NDA. Thus, on Reliant’s theory, had the TriCor micronized capsule formulation been approved under a separate NDA, Reliant would have been permitted to avoid certification as to any patents listed for the micronized formulation (even though Reliant apparently performed its bioequivalence testing against that product). Conversely, under Reliant’s theory, if the tablet covered by the patents in dispute here had been approved pursuant to a supplement rather than a separate NDA, Reliant would have been required to certify to those patents. That is an absurd result. Nothing in the statute or its legislative history suggests that the important patent certification requirement was to be determined by the happenstance of whether a supplement or a separate NDA was the vehicle for approval of a new formulation.

## CONCLUSION

Three separate formulations of TriCor, fenofibrate tablets, micronized fenofibrate capsules, and non-micronized fenofibrate capsules, were approved by FDA on the basis of exactly the same preclinical and clinical studies. The preclinical studies were conducted using the fenofibrate drug substance and the clinical studies were conducted using the non-micronized capsules.

Reliant now seeks to rely upon the same studies for approval of its micronized fenofibrate capsules product. The FFDCAs mandates that Reliant certify as to all of the patents listed for each of the three formulations of TriCor approved on the basis of these

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<sup>8</sup> Even using Reliant’s referent to “on” rather than “for,” this is inaccurate with respect to the animal safety studies, which were performed “on” the active ingredient.

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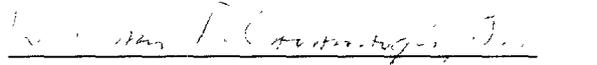
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studies. Because Reliant has repeatedly refused to certify to the patents properly listed for Abbott's NDA 21-203 (fenofibrate tablets), approval of its NDA 21-695 must be denied.

For all the reasons stated here and in the original petition, the petition should be, in all respects, granted.

Respectfully submitted,

  
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